FIG. 1.

Fig. ... a ... ution of telangiectases on cheek, lips, ear, nose and eyelids.

Tongue ... Showing lesions on anterior portion of tongue. Angiomatous lesion on lip bled profusely ...

Nasal Section ... Showing telangiectatic lesions on septum. The anterior one bled very profusely.

Finger ... c. Lesion under finger nail bled once or twice.

INTERNATIONAL CLINICS

A QUARTERLY

OF

ILLUSTRATED CLINICAL LECTURES AND
ESPECIALLY PREPARED ORIGINAL ARTICLES

ON

TREATMENT, MEDICINE, SURGERY, NEUROLOGY, PÆDIAT-
RICS, OBSTETRICS, GYNÆCOLOGY, ORTHOPÆDICS,
PATHOLOGY, DERMATOLOGY, OPHTHALMOLOGY,
OTOLOGY, RHINOLOGY, LARYNGOLOGY,
HYGIENE, AND OTHER TOPICS OF INTEREST
TO STUDENTS AND PRACTITIONERS

BY LEADING MEMBERS OF THE MEDICAL PROFESSION
THROUGHOUT THE WORLD

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MEDICINE

MEDICAL QUESTIONNAIRES

THE 1930 BRITISH MEDICAL ASSOCIATION MEETING IN WINNIPEG, CANADA

LIST OF ILLUSTRATIONS TO VOLUME IV

(FORTIETH SERIES)

COLORED PLATE

FACE.—Showing location of telangiectases on cheek, ear, nose, and eyelids.

TONGUE (a).—Showing lesions on anterior portion of tongue. The angiomatous lesion on tip of tongue bled profusely at times.

NASAL SEPTUM (b).—Showing telangiectatic lesions on septum. The anterior one bled profusely at times.

FINGER (c).—Lesion under fingernail bled once or twice.

[*Frontispiece*, Fig. 1, page 255

PLATES AND CHARTS

Clinical Papers from France [*]

BOILS AND CARBUNCLES: THEIR TREATMENT BY OXYGEN

By ASSISTANT PROFESSOR DE KEYSER, M.D.

University of Brussels, in the service of Professor Gougerot, in the Clinic of the Hospital of St. Louis, Paris, France

THE furuncle, familiarly known as the boil, and the carbuncle constitute in reality but two manifestations of the same affection. Thanks to bacteriology, the cause of these lesions, which are sometimes so different in appearance, has been isolated and this puts the question of etiology and therefore of nosology beyond doubt. Formerly, the carbuncle was considered to resemble so closely the virulent pustule due to anthrax that the differential diagnosis was hard to make. The discoveries of Davaine and Delayre and the isolation of the staphylococcus have made a precise distinction possible. A carbuncle is only an agglomeration of boils which result from the attack of staphylococci which have succeeded in gaining a foothold in a group of hair follicles or sebaceous glands. More rarely the seat of the infection is a sweat gland, or still more rarely, a ceruminous gland in connection with the auditory meatus, where it may be very painful.

The lesion, whether it be a simple boil or a carbuncle, is due to an external infection which has a definite contagious element in it. It is often inoculable and I find it necessary to emphasize the rôle that this process plays in this affection, either directly by the hand when the patient insists on squeezing a boil already present or by the shirt collar, especially when that has been roughened by usage and laundering. There is no doubt that the affection occurs less frequently among men since fashion has demanded the use of collars that are wide or soft. On the other hand, among women who now have

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[*] The following three articles were kindly secured for insertion in the INTERNATIONAL CLINICS by Dr. James J. Walsh, of New York City, during his recent trip abroad, and were translated and edited by him for publication.—EDITOR.

recourse much more frequently to the hairdresser since they have had their hair cut short, boils on the back of the neck have become much more frequent than before. Indeed, they are noticed more commonly all along the line of the hair. Wherever there is an opportunity for external irritation in the presence of dust, boils are likely to be noticed, and when patients lack resistive vitality or when there is persistence of the irritation, the single-follicle boil may readily become the many-follicle carbuncle. Certain professions predispose to the occurrence of boils in locations where their occupation tends to expose the subject to infection. Boils, for instance, are rather frequent, or at least much more frequent than among other people, among those who ride horseback and those who bicycle a good deal.

I insist a good deal on this rôle of local irritation in the production of boils and above all on their auto-inoculability because physicians very often attribute the occurrence of furunculosis to constitutional causes and draw an argument from this assumed etiology to weaken patients by dietary restrictions which are often too severe. The rôle of the constitutional condition in the production of boils is real, and some patients suffer from furuncle after furuncle, never apparently acquiring any immunity. Not infrequently in these cases patients have the unfortunate habit of applying topical applications of one kind or another which lower very seriously the resistive vitality of the skin and multiply both the causes and opportunities for inoculation. The wet dressing is, of itself, often to be deprecated and is responsible for re-inoculations, for while it diminishes the inflammation, it is often too moist and disseminates the staphylococcus by the fluid which flows from it. The bath is equally dangerous for the same reason and multiplies the opportunities for dissemination, both for the patient himself and for other bathers when there is a public bathing place or pool.

The symptoms of furuncle or furunculosis are well known. I wish to call special attention only to the furuncle on the upper lip which must always be considered rather serious and carries with it a ligneous infiltration of the tissues. As a result, the upper lip sticks out disfiguringly and painfully and the lower lids may become affected by the edema, so that the patient can scarcely open his eyes. If suppuration occurs promptly, the evolution of the furuncle comes rapidly to an end, but if, on the contrary, the opening is only a very

small aperture, the evacuation of the pus may be slow, the edema augments, a network of veins makes itself manifest and there is then grave danger of phlebitis of the facial veins. This may be followed by thrombophlebitis of the cavernous sinuses, followed by death in two to four days. The condition must never be considered lightly and the patient must be warned of its dangers and when it occurs in children, parents must be told of its possible seriousness. The treatment must not be neglected and proper opening must be made just as soon as pus declares itself.

A word, besides, with regard to diffuse carbuncle of the neck, and especially the back part of the neck. It is rather rare and it attacks particularly individuals who are debilitated by age or by illness. It is accompanied by systemic symptoms which are sometimes very intense, with an elevated temperature and locally a hard tumefaction which has acquired for it the name of ligneous phlegmon, or woody infiltration. When suppuration occurs there are a series of purulent openings and some subcutaneous burrowings. Very often the general health declines and septicemic symptoms intervene, followed by death. A fatal termination, however, may occur as the result of a secondary hemorrhage consequent upon ulceration of a blood-vessel. These serious complications are likely to occur only where there is sugar or albumin in the urine in considerable quantities or other symptoms of disturbance of metabolism.

Such accidents are happily rare in the strictly local affections called the boil or furuncle. The therapeutic indications for the treatment of boils are simple enough and may be deduced from the condition itself. Above all, the treatment should be local, but we should besides try in every way to strengthen the patient and ameliorate the constitutional condition which he presents and which may need special attention. Brocq, years ago, praised very highly the value of fresh beer yeast for the constitutional treatment of patients with a tendency to suffer from boils. The salts of tin were also highly lauded for this same purpose. I am free to confess that I have been completely disillusioned with regard to these remedies and the lack of results which have been given by these methods. Vaccino-therapy appears more useful and apparently provokes in the fluids of the body the apparition of new substances, the precipitines, the bacteriolysins, the agglutinins and the opsonins which

represent valuable reactions against the infection. If it is impossible to obtain an auto-vaccine, one may employ a stock vaccine, and especially one that is made by an association of the yellow staphylococcus with the white staphylococcus and other bacteria to the extent of some six billions of germs to each cubic centimeter.

The manufacture of the vaccine must not destroy the microbes destined to cause the vaccinal reactions, for then they would not produce antibodies and would fail of their purpose. They are deprived by different procedures, however, of the faculty of reproducing themselves. The question might readily occur, how can the vaccine act if the infecting microbe does not produce by itself its immunity? I think that it is because the vaccines are introduced into the general circulation, while the microbe itself remains localized in the hair or sebaceous gland apparatus in which it first began to multiply. I have tried practically all the vaccines from all the countries and the results have not been what I hoped for and good effects have been inconstant and not to be relied upon. Especially the bouillon vaccine of Delbet failed in my hands and it seemed to have a shock activity rather than a specific therapeutic effect.

We must depend, as a rule, on the local methods of treatment.

A good deal of praise has been given to the method of aborting a furuncle by phenic or carbolic-acid sprays or by spraying with iodo-acetone or corrosive sublimate one to one hundred. Others have recommended the wet dressing with carbolic acid or with alcohol. If the furuncle continues to develop in spite of these measures, one must have recourse in general to surgery employing either the bistoury or the thermo-cautery to evacuate pus. As a rule, a crucial incision is made followed by scraping, or some surgeons have gone to the extent of excising the furuncle or boil as they would a tumor. I wish to say to you quite frankly that I find this practice useless. It is very painful and does not shorten by a single minute the evolution of the lesion. To ask the surgeon not to do this is to demand too much; for most surgeons the idea of furuncle creates at once the reflex, bistoury, though, almost needless to say, if this be used it will be at the price of a cicatrix, which is often very disfiguring.

For the past thirty years I have watched one after the other of these methods fail in the treatment of furuncle and I have employed oxygen therapy. This is not my own invention and all that I have

done is to modify the technic of Professor Thirair, who, in November, 1899, made a communication on this subject to the Academy of Medicine of Belgium. Thirair treated all infections by oxygen, not only uterine infections but also those of furunculosis and of carbuncle. In his service a special set of tubing carried oxygen to every bed. In the neighborhood of Liége the miners of Borinage suffered rather frequently from what they called the "black button." This was a severe furunculosis, due to their occupation, which compelled them in a number of cases to abandon their work. The application of the method of Professor Thirair (that is, the oxygen treatment) furnished some very brilliant results among his patients. The gas was compressed to 120 atmospheres in a metallic cylinder and was used by means of a needle which carried the gas directly into the infected tissues. The flow of the gas was regulated very simply by noting the escape of bubbles when the needle was plunged into a glass of water. A single injection may be continued for several hours.

Almost needless to say, this infiltration with gas of an inflamed tissue which is already tightly stretched is very painful. Besides, it is necessary to repeat the needle pricks whenever the needle gets blocked or produces an opening through which the oxygen flows regularly. The method of Professor Thirair gradually fell into desuetude by reason of its inconveniences and perhaps also because the medical fashion carried physicians away to other procedures.

What I have done, then, is to take up and simplify the method of my Belgian master. I never make permanent injections when I do not see the necessity for them. I never make openings into unbroken tissues and I make use of needles introduced into the opening of the furuncle itself. Whenever this opening is delayed, I hasten it somewhat by the application of wet compresses which have been wrung out in oxygenated water or solution of hydrogen peroxide. This procedure is entirely without pain. If the needle is introduced into one of the orifices of a carbuncle, it is easy to see a sanguinolent puriform material coming out of the other openings. This is an indication that the oxygen is finding its way through the burrowings of the furuncle or carbuncle. For a large open wound the application is made directly, the gas coming through a tube applied to the skin.

My own experience has been that after three or four applications have been made, the furuncle is cured in three to four days. I have never seen any complication and the result is better than in cases which are favorably influenced by the bouillon of Delbet; for the employment of this—three injections made every two days—demands a week to complete the treatment. Carbuncle is slower to cure but the cicatrization takes place in fifteen days. It would be interesting to cite for you a series of observations but I shall only describe for you a few cases.

The first patient to whom I shall call attention was a man of some sixty years of age who developed a carbuncle between his shoulder blades. A surgeon treated this by excision. The cicatrization was interrupted by further surgical intervention and required altogether three months. Not long afterwards his wife came to me for the treatment of a carbuncle that was still quite solidly infiltrated and had no openings. I advised wet dressings and as soon as an opening occurred I made five applications a day with oxygen. The opening remained single and the pus which flowed from it came away freely. No other aperture formed and in fifteen days the cure was complete without cicatrice or complication.

The second case was that of a man of forty-five, the brother of a physician, who presented himself with a profuse carbuncle of the neck. I have already told you of the seriousness of these. There was actually some extension of the purulent condition down the back and a very much debilitated constitutional condition with high albuminuria. The patient's brother picked away each day with a pincers the portions of tissue that had mortified and applied with great care antiseptic dressings. When I was asked to see the case, I suggested the application of oxygen through the needle and at the end of three weeks the patient was able to be around and at the end of a month was once more able to take up his occupation.

The third case is that of an old man cured in the same way in three weeks of a diffuse carbuncle. The cure occurred without rapid elimination of pus and without the formation of new foci of infection.

What is then, according to our present ideas, the mode of action of the oxygen? Does it destroy the *staphylococcus aureus*? It does no such thing. This microbe is aërobic and its cultures are neither arrested nor retarded by the passage of a current of oxygen through

them. In spite of this, this particular microbe, the *Staphylococcus aureus*, disappears rapidly from the furuncle which has been treated by oxygen. Jarris and Willems have demonstrated this by laboratory tests. They have shown that successive plantings in the furuncle treated with oxygen give fewer and fewer positive results in the bacteriologic laboratory. Without doubt, the oxygen brings about an augmentation of the phagocytic power of the white blood-cells. As a result, the purulent condition is overcome and the tendency of the tissues under the influence of the *Staphylococcus aureus* to mortify is largely overcome.

Besides, the oxygen method exercises a systemic activity on the organism. This is clear from the fact that there is from the hematologic point of view the development of a relative leukopenia during the course of the lesion. At the beginning of the development of the furuncle there is produced, as a rule, a neutrophil polynucleosis. This manifestation under the influence of local oxygen therapy falls soon to rather low figures distinctly below the normal. Among the mononuclear elements, on the other hand, there is a relative augmentation of the lymphocytes and of mononuclear or medium-sized cells besides a diminution of the granular matter within the cells.

One cannot help but be struck by this diminution of the leukocytosis of defense, especially as one would be inclined to think that an augmentation would occur. It would be hazardous to affirm that this modification indicates the increased activity of the white cells which we owe to the oxygen injection.

Without explaining by hypothesis the success of the method, oxygen therapy is the most painless and at the same time the most efficacious of all forms of treatment for boils and carbuncles. Lesions of this kind are becoming so much more common in the midst of the dusty, industrial life of cities, due to the ease with which infections may take place and above all as the result of the baths, public and private, which are now so much more common than they used to be, that it is well to have at hand a mode of treatment that promises to to save our patients pain and at the same time prevent the development of serious complications.

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indubitable, but as a simple hypothesis. The facts which I am about to present to you, facts that are well known and of indubitable veracity, will make it very clear that it is not a hypothesis but a veritable doctrine of medicine with which we are concerned. Even the most incredulous will, I think, be persuaded of this, when we have come to the consideration of the facts that I wish to present.

About the beginning of the present century it became the custom in certain hospitals of Paris to make a systematic examination of the lungs of all those who had died in the hospital, no matter what the disease to which they had succumbed. This postmortem examination revealed that about 95 per cent. of all the bodies presented lesions of tuberculosis, the greater part of them perfectly cured and cicatrized. If one only recalls that the *Bacillus tuberculosis* is not limited to attacks upon the lungs but may affect most of the other organs of the body, it would not be too much to think that practically all of these patients have at some time or other been sufferers from active tuberculosis. We are all a little tuberculous. Now the immense majority of us have never had the slightest suspicion of this susceptibility to tuberculosis and its actual occurrence. The microbe was conquered without any external help and the organism itself proved quite capable without external aid of any kind in setting the bacillus in a condition where it is incapable of injuring us.

This fact, it may be said in passing, justifies very thoroughly the expression of Professor Grancher, "Of all the chronic diseases tuberculosis is the most curable." I have had the opportunity on many occasions to bear witness personally to the perfect exactitude of this affirmation. I am happy to say it once more if only in order to reassure those who very wrongly imagine that tuberculosis is an incurable disease.

Let us take another example. Here is a village of a thousand inhabitants whose sole water supply becomes contaminated by the bacillus of Eberth, the microbic cause of typhoid fever. If the presence of the bacillus is sufficient to bring about the disease of itself, all the inhabitants without exception will be stricken with typhoid. But will anything like this happen? Evidently not. Out of these thousand inhabitants, thirty or forty perhaps will be stricken with the disease and the others will remain perfectly immune to it. The great majority of them have been protected then quite beyond their

DEFENSE AGAINST DISEASE THROUGH THE NERVOUS SYSTEM

By MARTIN du THEIL, M.D.

Neuilly-sur-Seine, Paris

To CONQUER disease is an excellent thing, but to prevent disease from securing a foothold in the human organism is infinitely preferable. There is no doubt that nature has gifted human beings with the weapons necessary to repulse without difficulty every attempt of microbic invasion. A normal healthy organism possesses in reality a veritable natural protector, an actual cuirass or coat of armor, if I may thus express myself, upon which the microbe can produce no effect, but let but the slightest fissure be produced in this defensive organization and disease finds its entrance into the body.

With very good reason it might be said that the best possible defense against disease-producing agents would consist in suppressing the aggressor. Evidently if there were no more microbes there would be no more disease. I am not sure that science will ever come to the day when it will be able to eliminate the host of microbes spread widely over the whole surface of the globe, some known, ever so many others still unknown, which are the natural foes of the race. One thing is perfectly certain, that the idea of getting rid of microbes is for the moment at least a purely utopian suggestion.

Nevertheless it is by this way that physicians are more and more tempted to limit their researches to the discovery of methods by which they will be enabled to destroy such and such a microbe in a patient. Would it not be better by a rational utilization of the natural defenses of the body to render all these microbes perfectly inoffensive? What significance does a microbe possess if his power of attack is rendered in advance impotent? Only a little attention on our part is needed in order to maintain in good state the all-sufficient defenses against disease with which nature has provided us. Above all I owe it to myself to prove the real existence of this natural defensive organization, for unless I do so the reader will have the right to look at my declaration not as an accomplished fact that is

indubitable, but as a simple hypothesis. The facts which I am about to present to you, facts that are well known and of indubitable veracity, will make it very clear that it is not a hypothesis but a veritable doctrine of medicine with which we are concerned. Even the most incredulous will, I think, be persuaded of this, when we have come to the consideration of the facts that I wish to present.

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Let us take another example. Here is a village of a thousand inhabitants whose sole water supply becomes contaminated by the bacillus of Eberth, the microbic cause of typhoid fever. If the presence of the bacillus is sufficient to bring about the disease of itself, all the inhabitants without exception will be stricken with typhoid. But will anything like this happen? Evidently not. Out of these thousand inhabitants, thirty or forty perhaps will be stricken with the disease and the others will remain perfectly immune to it. The great majority of them have been protected then quite beyond their

own knowledge and the attack has been repulsed without their having had the slightest suspicion that a great victory over this disease is being won within them.

One could multiply examples like this almost endlessly, always with the same results. There is no doubt this immunity on the part of certain persons points to the existence of a natural defensive organization quite sufficient of itself in the great majority of cases to reduce to impotency without any external aid every attempt at invasion on the part of disease. It is now established that the microbe is only the occasional cause of disease whose attack is without effect on the organism if that is in healthy equilibrium. The good state of the health depends exclusively on the maintenance of this equilibrium.

Hence the expression of our great French physiologist, Claude Bernard, to whom we owe the initiation of our knowledge of the endocrine glands: "The microbe is nothing; it is the condition of the system on which the microbe secures a foothold that counts for everything—*le microbe n'est rien; c'est le terrain qui est tout.*"

We live in reality in the midst of enemies and especially of microbes which attack us incessantly. The human body is a veritable battlefield. The struggle, and it is very really a struggle for life, is constant, but in a healthy organism the victory is also constant. To the vigor of the attack responds the vigor of the defense, and so is found realized a perfect equilibrium.

These natural defenders we know very well now; they are the white blood-cells called also phagocytes, because of the curious phenomenom known as phagocytosis in which they take part. But these leukocytes are only soldiers, executive agents, and it is important to realize that they owe their activity to the condition of the body and to the vitality which it has as the result of the equilibrium of the nervous system. The defense machine is perfect but it needs an animator and that is secured through the nervous system and especially that part of it that is known as the great sympathetic.

This animator of the human machine exists in actuality and is bound up with a single set of tissues in the organism, that is with the nervous system or rather with that part of the nervous system called the great sympathetic. The great sympathetic is a mysterious organ which plays an important rôle in the human economy, presides

over nutritional changes, provides for reaction against systemic fail-
ures of various kinds, foresees the needs of various organs and affords
relief to those which are threatened in any way. It represents at once
the intelligence which presides over the body and the force which
executes what is necessary. It is the supreme animator of the system
and it is in it and it alone that resides the secret of life. If the
white blood-cells may be looked upon as the soldiers of the body,
then the great sympathetic may be looked upon as the general-in-chief
which marshals the forces and rallies them wherever they are needed.
We shall talk first of the soldier and then of the general-in-chief.

What is a leukocyte or white blood-cell? Physiology teaches us
that it is a white cell or leukocyte which is really a little organism
constituted by a protoplasmic mass with one or more nuclei. It pos-
sesses the faculty of sending out prolongations called pseudo-pods
which permit it to change its form, to move from place to place and
even to find its way through the walls of blood-vessels or lymphatics
which constitute its habitual residence. Every cubic millimeter of
blood contains eight to ten thousand of them. That is an insignificant
amount compared to the red cells which exist to the number of about
five million in every cubic millimeter.

These white cells are of great importance in the defense of the
body against microbes. Whenever the white cells have fought a
winning battle with a particular kind of microbe, they receive the
power to destroy all microbes of that kind henceforth without a con-
test. That is the principle of vaccination and Metchnikoff's doctrine
of phagocytosis enables us to understand that the defense of the body
against disease consists in the phagocytic power of the white cells.
In recent years we have learned that the vitality of the phagocytes
depends very largely on the condition of the nervous system and
that under conditions of discouragement or despondency the leuko-
cytes fail to have the resistive vitality against disease which they
possess under normal conditions. While the leukocytes are so impor-
tant then, their power depends to a very great extent on the condition
of the nervous system so that the defense of the body against disease
is largely a matter of the potency of nervous impulses.

It is not with the cerebrospinal nervous system that we are
concerned here, for that is occupied mainly with movements and sen-
sations, and the only thing that concerns us here is the great sympa-

thetic. The great sympathetic, it may be recalled, is constituted by a double chain of ganglions bound to each other and located on both sides of the vertebral column. From these ganglions emerge numerous nervous branches which terminate in the organs that preside over our vegetative life. Their terminals are in the liver, the spleen, the lungs, the heart, the stomach and intestines, as also the ductless glands. They form in certain regions veritable networks called plexuses and they provide for communication between the great sympathetic and the central or cerebrospinal nervous system.

The nervous system is the motor, as it were, of the human machine. Every machine needs a force to set it going but this must not be a blind force. It ought to be intelligent in order to set the machine going as well as to maintain it in action. The chauffeur guides the machine in such a way as to avoid obstacles, but he must also watch attentively over the various parts of his mechanism for any defect that will hamper or bring about the stoppage of the functioning of the machine.

My first experience with the value of this method of treatment by devoting the therapeutic attention to the nervous system, not only for the prevention of disease but also for its cure, came during the grippe epidemic which followed the Great War. When I was demobilized in the fall of 1918, I returned to Neuilly just when the awful grippe epidemic made its appearance there. I was led to realize from the beginning that the persons who were most seriously stricken by the affection were in general young women, and especially young married women. I soon came to realize the reason for this. Separated from their husbands since August, 1914, except for the rare intervals when their husbands were on leave, these young women lived in a perpetual anxiety and amid the constant expectation of bad news. When the long-looked-for letter came it was scarcely read before the anxiety returned that perhaps the signature was only just dry before her husband had been killed or badly wounded. Their nervous systems exhausted by these severe trials left them without defense against microbic invasion. Without hesitation, then, tracing back from effect to cause I concentrated all my efforts on the nervous system so as to make these patients face their ills with as much courage as possible. My success was so complete that I had the satisfaction of not losing a single case. This result would have sufficed

to sweep away all my doubts if I had any left and after this I did not hesitate to proceed in the same manner in treating without exception all affections of an infectious nature.

Above all in the two diseases which are the most serious for mankind at the present time, tuberculosis and cancer, I found that this method of treatment was of very great efficacy. The effect of the state of the nervous system on tuberculosis is very well known. A generation ago it was the custom to talk of tuberculosis as hereditary and a great many patients afflicted with the disease were inclined to think of themselves as doomed. This was particularly true if they had seen other members of their family die from the disease. Then came the recognition of the fact that tuberculosis was really a contagious disease and that whatever hereditary element, if any, was in it, was very slight. As the result of this new attitude toward the disease, it became much easier to lift patients out of a state of despondency into which they were inclined to sink, and give them new courage and hope which, acting through their great sympathetic, enabled them to resist the encroachments of the disease and prevent its further progress at least.

As the result of this we have found tuberculosis to be a very curable disease and indeed when it is treated properly it justifies very strikingly the expression of Professor Grancher to which I called attention before, "Of all the chronic maladies, tuberculosis is the most curable." Personally I am very much inclined to think that the gathering together of numbers of tuberculous patients in sanatoria is not good for them. I may say quite frankly and without ambiguity that I am an enemy of the sanatorium and I consider the environment which is created by having large groups of these patients gathered together as quite unsuitable for their improvement and cure. Everything about the patient, unfortunately, recalls to him the reality of his disease if he were at all inclined to forget it. On the other hand I am strongly in favor of country life far from the noise of the city and its trials and preoccupations as beneficial for the tuberculous patient. This quiet and contentment enables the nervous system to recover its energy and stimulates it to struggle with success against infection even when the bacilli find themselves firmly implanted. The success which is secured by these means

represents a strong argument for the thesis as to the action of the nervous system over the disease.

Not only in tuberculosis, serious disease that it is, but also in that still more serious affection, cancer, the question of the influence of the nervous system is extremely important and yet unfortunately has been neglected. In this above all it is important to remember the aphorism, "The microbe counts for nothing; it is the soil (terrain) which counts." How many evils would have been spared humanity if this aphorism had only been recognized at its true value and the path indicated by it followed.

If there is any disease which shows in most evident fashion the importance of the soil or terrain, and as a result the influence of the nervous system, it is cancer. This is the name under which are assembled all the malignant tumors, and yet there is probably no disease in which the place of the nervous system is so much neglected as cancer. Cancer does not break out suddenly like a pulmonary congestion but, on the contrary, slowly, and develops but gradually, so that nature would seem to want to warn us a long time in advance of the necessity for defending ourselves. Probably no reader of these lines is without the experience of having known or had as a relative a victim of cancer. I appeal to him, then, to recall whether he does not recognize the truth of the statement as to the occurrence of advanced signs which constitute a veritable alarm signal of approaching malignant disease.

Without talking of particular signs, variable according to the localization of the tumor, one remarks always during a long period, weeks at least and often months, manifest symptoms of the deterioration of the nervous system. Often a general fatigue appears at the beginning without any apparent cause and which ordinary means fail to cure. Sometimes the appetite is disturbed, but whether it is or not the patient grows thin. Soon it is noticed that he becomes taciturn, is rather easily discouraged, and while on questioning he does not reveal any localized symptoms of disease and usually has no real pain, he complains of an undefinable malaise or failure of strength.

Then the patient's color begins to be modified under the influence of the poison which infiltrates by degrees through the system and the resistance decreases. Those who know him best find that he does not

look well, and they sometimes translate their impressions in a familiar but very expressive phrase, "There is probably something inward the matter with him." As time goes on, all the symptoms become accentuated and the strength diminishes more and more. The great sympathetic without any special assistance is obliged to furnish during this incubation period extra resources and grows feeble under the effort. The white cell defense diminishes from day to day while the invader's power of attack increases. Finally the enemy is installed as master in the organism though even slight aid to the nerve cells brought at the beginning would have sufficed nearly always to repulse the invader. The multiplicity of these warning signs that are noted in such cases demonstrates beyond all doubt a definite preponderating influence of the nervous system in the evolution of cancer.

There is another fact that to my mind is of capital importance and shows the danger which follows an excessive waste without compensation in the nerve cell. So far as I know, no one else has ever called attention to it. It is a fact that cancer is just that much more frequent according as the environment is more cultivated. Among the working classes in towns and fields, absorbed as they are almost entirely by the physical labors to which they must give themselves in order to gain their livelihood and that of their families, cancer is, if not exceptional, at least rather rare. Just in proportion as people advance in culture and in the social scale, cancer augments in frequency and one finds its full development among those who give themselves most to intellectual work of various kinds. The relation of cause and effect is thus definitely established. Excessive waste uncompensated in the nerve cells brings on a disturbance of vital equilibrium. The diminution of the energy of the nervous system reacts upon the resistive vitality and the infectious agent finding itself in the presence of insufficient resistance triumphs in the end. So far as I can see there is no proof more decisive than this of the fact that in order to be preserved from cancer as well as from the various microbic diseases, we should not depart from the path which Claude Bernard pointed out to us. To maintain the resistive vitality, that is the soil or terrain on which the microbes grow, at its highest vitality is the best preventive. On an organism

whose nervous system is in perfect equilibrium, microbes are not able to gain a foothold.

The question then may be summed up thus: Are we physicians sufficiently equipped by the advance of medical science to maintain this equilibrium of the nervous system even where microbes have begun their invasion? There is no doubt that the answer is yes. Even as regards cancer, I am quite sure that the maintenance of nervous equilibrium is sufficient to protect the individual. My conviction in this regard is absolute. It does not rest on simple hypothesis but on very definite observation and experimentation. My conviction comes from the treatment of patients suffering from some of these tumors that are called benign, such as fibromas, polyps and the like, whether the tumor has been operated on or not. It is well known that tumors of this kind rather readily evolve in the course of time into a cancerous form.

Now among these different patients carrying tumors that were so likely to degenerate malignantly, I have found that after proper treatment of the nervous system not a single case of cancer has been noted. If this observation of mine had been made only over a period of two months, I should not speak of it at all or I should be careful to keep from drawing any definitive conclusions, for after all that might be due merely to a simple coincidence, but since this experience of mine is founded on a period of more than ten years, as is the case, it is no longer possible to talk of coincidence and it would be to deny the value of evidence entirely to refuse to acknowledge the reality of a preventive action so manifest as this. For me no doubt any longer exists. I have a profound conviction, a conviction that is founded on reason, resting not on theory but on fact, that one can prevent the occurrence of cancer and I do not hesitate to say that I have obtained excellent results in this matter.

There is another argument of even more significance in favor of the action, curative as well as preventive, of the nervous system in the matter of cancer. I know how true it is that I am saying nothing new that the prognosis after an operation for cancer has become more and more unfavorable since a fatal relapse has become almost the rule, one might say, it occurs so frequently. Now during the last ten years since I have made it a point to submit all my patients who have been operated on for cancer to a systematic treatment cal-

culated to secure equilibrium of the nervous system, I have not had to note a single relapse. This refers not only to cases of recent date, but to those also who have passed years in comfort and without relapse. One of my cases dates from the end of 1918. May I be permitted to say that there is one relapse, but even in this case the outlook is most hopeful, for the tumefaction which occurs with the relapse is of an entirely different appearance from that for which surgical intervention was demanded and this tumor has been removed without difficulty and there is no longer any sign of glandular involvement. More than this, and I attach to this sign a great importance, the terra cotta pallor of the patient before the operation has disappeared and given place to a clear, normal complexion attesting that the disinfection has been accomplished. This provides me with one very good reason for giving a favorable prognosis to this question.

I want it understood that in my statistics of cases I do not give place to any case where the cancerous nature of the tumor has not been verified by proper pathologic investigation. Before concluding this subject I must permit myself the satisfaction of mentioning a special case, the seriousness of which makes it of great interest, and I mention it if for no other reason than in order to show that one must never give up hope in these cases.

One of the most eminent of the surgeons of our hospitals here in Paris will not fail to recall it if I mention the case of a cancer of the intestine which he operated upon in one of my patients. This was a cancer of the worst form with numerous glandular involvements. The surgeon, well known for his professional conscientiousness, considered the case so serious that he had, as he said to me, almost regretted the infliction on the patient of the additional suffering consequent upon the operation. The removal of the tumor he felt after the operation could give to the patient only a very short period of survival, two or three months at most. Fortunately this male patient was extremely docile. I insisted on a régime that would maintain nervous equilibrium. At present almost five years have passed since the operation. The patient has watched his weight increase by nine kilos (more than twenty pounds), his color has become normal, he presents all the signs of good health, and those who know him the

best are quite ready to declare that he has never seemed in better health.

In conjunction with these physical therapeutic measures, it is extremely important to put the patient in as good a state of mind as possible. There is no doubt at all that direct action upon the morale of the patient can augment notably the activity of the remedies and restore the nervous equilibrium for purposes of resistive vitality. In order to secure this, the physician must have the fullest confidence of the patient and the physician's first care must be to secure that. To obtain that a very careful examination of the patient must be made so as to make him or her feel that no possible source of the symptoms can escape notice. It must not be forgotten, however, that patients suffering from chronic affections are frequently the subject of more or less emotional crises and that this is particularly likely to be true on their first consultation with a strange physician. To question them too meticulously under these circumstances is always a mistake, for they are prone either to attenuate or to exaggerate their troubles. It is extremely important, then, above all, to set the patient's mind at rest and dissipate his apprehension and secure his confidence. Once this result has been obtained, the real examination of the patient can be pursued with advantage and can be made with minuteness so that every organ will be properly investigated. The examination should be made in detail, not forgetting how often reflex troubles are noted; how often, for instance, patients whose complaints are always with regard to their stomach, so that they seem to be suffering from intractable gastritis, are really the victims of an unsuspected chronic appendicitis.

Even after the diagnosis has been made and he is ready to prescribe, the physician's rôle in the case is not at an end. I would even say that the most delicate and the most decisive part of the duty that he has to fulfil remains. The patient has come in order to be cured and the first condition for that is evidently that his physician's advice should be followed faithfully. Very often the patient is the subject of discouragement. Let us take the example, for instance, of a tuberculous patient who for a long time has lost weight, coughs, loses his strength. His physical condition reacts upon his moral condition until, haunted by the idea of this disease which he imagines to be incurable, he will be tempted, if he is left entirely to himself,

to abandon hope and to give up the struggle. The duty of the physician is then to transform radically the patient's state of mind and for that he must not merely make an impression on him, but he must convince him of the probability of cure. The physician must show him that the cure which he despairs of is, on the contrary, within his grasp and depends henceforth entirely on his own will. Polite agreement on the part of the patient with the reasons that are given him is not sufficient. It is necessary to produce on the patient a genuine conviction lasting and effective. Only the fullest persuasion accomplishes that. For this purpose, the physician must proceed with gentleness, without harshness, being careful to avoid scaring the patient. It is important while conversing with him to abstain from using technical terms of which the patient may not know the significance, for he is always tempted in this case to interpret what he hears in an unfavorable sense.

After having shown the patient the essential cause of his disease, and that it is due to a passing insufficiency of his natural defense against disease, the physician should always be able to make the patient understand how the treatment will react to make up for this insufficiency and give him back his health. It is for this reason that I think it useful to give to the remedies which I employ a name which recalls every time that they are taken the action proper to each one. This is a little thing in itself but when there is question of exercising an influence on the nervous system, who would dare say that it is so slight as to be negligible?

With the same thought in mind, I consider it very useful to have some person who is closely intimate with the patient assist at the consultation and listen to the explanation or the conviction which this person will have received in this way, will give him or her particular influence for good over the patient. Those who live in the immediate environment of the patient can produce a very precious effect in maintaining the patient in such a state of confidence as will benefit him and maintain in him that hopefulness which it is so important to give back to him. I would say that one ought to create about the patient a veritable atmosphere of confidence with which he will be literally and continuously impregnated. Now an influence of this kind can be exercised only as the result of a real conviction and never from any pretense, for the patient will always detect that.

I make use of the psychic action in all my patients without exception, even in those cases where the physician must yield to the surgeon for a time at least. Surgical intervention is always serious and we ought not to have recourse to it except in cases of absolute necessity, but when, after a minute examination, renewed if necessary, the physician comes to the conviction that surgery would be helpful, he ought, apart from all self-interest, think only of his patient and advise recourse to the surgeon. Under these circumstances I think that it is extremely important to keep the mind of the patient as confident of cure as possible and above all to lessen his apprehension, for this will add greatly to the prognosis of the surgical intervention.

The experience with tuberculosis has been a very precious lesson in this regard. In the days when patients thought the affection was hereditary and therefore hopeless of treatment, the death rate was high because of the discouragement and the lack of morale which led to disturbance of the nervous equilibrium that supports resistive vitality. Just as soon as that idea of heredity was dissipated, patients began to get better in much larger numbers, until, as I have said, Grancher's aphorism became true, "Tuberculosis is the most curable of diseases."

Unfortunately at the present time with regard to cancer, there is being created more and more in the minds of patients the feeling that their disease is incurable, that relapse is almost inevitable and the most that they can hope for is three years of life. Under these circumstances the soil or terrain on which the cause of cancer, whatever it may be, implants itself, is seriously disturbed. It proves incapable of exercising that resistive vitality which would enable it to throw off the cancer invader, whatever its nature may be. It is easy to understand under these circumstances that unless patients can be brought to a better state of mind, their resistive vitality is very much lowered and relapse becomes almost inevitable.

It is easy to understand from this that both before and after operation, patients ought to be brought into a state of confidence as absolute as possible with regard to the cure of disease or relapse as almost inevitable. Everyone realizes that at the present time there has been so much talk about cancer and its fatality; above all the increase in the number of deaths from cancer and the fre-

quent discussion in the newspapers of the ever greater scourge it is becoming discourages patients very much until they are prone to have very little serious hope of the cure of their condition. Under these circumstances the mortality is ever so much higher than it would otherwise be. This question of the defense of the organism through the nervous system becomes of the greatest possible significance. While the search for the physical cause and prevention goes on, the question of the support of the nervous system and the maintenance of the equilibrium of the great sympathetic in order to enable it to accomplish its purpose of increasing the resistive vitality must come to be looked upon as the most important of measures in the therapeutics of our chronic diseases.

The formula which I use for the purpose of conserving in the great sympathetic the energy necessary to maintain resistive vitality against microbic infection is the principal part of my therapeutics. Its one purpose is to maintain always intact a reserve fund of energy from which the cell may draw whatever is necessary for compensation for its expenditures. It plays in a certain sense the rôle of an alimentary nutritive for the nerve cells. The prescription is as follows:

℞
Arrhenal (an arsenical preparation) .... 0 gram 025
Tincture of nux vomica .... 0 gram 10
Alcoholic extract of yellow cinchona .... 0 gram 0666
Aqueous extract of red cinchona .... 0 gram 0666
Sodium glycerophosphate .... 0 gram 333

This is the amount contained in each spoonful and though the dose is relatively feeble the activity of the mixture is really remarkable. I attribute this particular action to the fact that the substances which make it up exert simultaneously the action appropriate for each one.

The human mind refuses to admit that nature could possibly have created this marvelous machine, the human body, without endowing it at the same time with whatever is necessary for its defense, and what simple common sense makes us prevision facts confirm. These defensive means are actually in us, they respond to all our needs, the nervous system keeps them under its direct and exclusive dependence, and it is only necessary to know how to use

them to put disease behind an unclimbable barrier. The conclusion from this is that in place of making war on such and such a microbe in particular, it is infinitely more simple, more logical and also easier to maintain the natural defenses of the body in good shape and the field of attack will then remain invulnerable to all the infectious agents without distinction. One thing that we must try to secure is that the microbe shall be put out of capacity to overcome our natural means of defense. At the beginning I quoted Claude Bernard's expression which cannot be repeated too often, the microbe is nothing, natural resistive vitality is everything. Physicians were inclined to think when the value of diphtheria serum was discovered that a whole series of serums would be found, but disappointment followed and we can scarcely hope to secure preventive vaccinations for every kind of microbe.

There has been a tendency to forget the significance of that wise axiom, "The laboratory helps the clinician and the study of clinical medicine, but does not replace them." Analysis is a precious means of investigation but nothing else. What ought to guide the physician is that primary principle that the most important thing in medicine is attentive observation, meticulous observation of every case, with regard to which I need scarcely say that no two cases resemble each other. The physician must constantly recall that ever veritable guiding principle, "There are no diseases but only patients." We must still confess and must never forget that medicine is an art and not a science and that the physician cannot establish a diagnosis as an algebraic equation. If we obstinately insist on combating each disease we lose sight of the marvelous means of perfection and defense of resistive vitality which nature has created in every organism. I affirm that in every normal organism all these natural means of defense are quite sufficient to enable the patient to overcome the disease. Prophylaxis is for all diseases and not for separate ones.

To say all in a single short sentence, no one ought ever to die except of old age.

RHEUMATISM OF DENTAL ORIGIN

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AMONG the many causes worked out for rheumatic affections, so-called, infections of the teeth claim a very special place. While their frequency as the etiological basis of the disease is certainly less high than has been claimed by certain authors across the Channel in England and still more across the Atlantic in America, this special etiology is not less peculiarly important to recognize because of the therapeutic sanctions it carries with it which are of themselves and very rapidly capable of bringing about relief of the symptoms and success in the treatment of the fundamental conditions causative of the disease. The medical history of this etiological connection is much older than is usually thought.

The distinguished American physician, Benjamin Rush, of Philadelphia, the signer of the Declaration of Independence, was the first in modern medical history to call attention to the existence of rheumatic affections of dental origin. It is quite true, however, that here and there in medical literature one finds, on looking back to the older times, certain observations which seem to show that these relations between the teeth and the joints had not entirely escaped the attention of older authors or even of ancient writers. In Hippocrates, for instance, there is found a clinical description of two patients in whom special attention to the teeth cured certain rheumatismal manifestations. As a matter of fact, however, one must wait for the time of Chaissaignac (1859) or Richet (1865) to get a clear expression of a cachexia consequent upon the teeth, or "buccal septicity." Galippe and the brothers Tellier insisted on this idea at the end of the nineteenth century but it is to Billings, of Chicago, Goldthwaite, of Boston, and Rosenow, of the Mayo Clinic, that we owe the idea which has today become classic in all the English-speaking countries of focal infection due to septic dental conditions.

In France, Frey, Rousseau-Decelle, Weton in the thesis of 192?, Ruppe, Lebedingsky, Mendel, Lagrange, Fargin-Fayolle, Nidergang,

and Peyre, as well as others, devoted themselves to the solution of this problem. In foreign countries, Buckley, Wilcox, Singer, Chvostek and others set themselves the same task.

The frequency of focal infection in the matter of rheumatism has been very differently estimated by different students of the problem. Dr. Anthony Bassler, the New York gastro-enterologist, calculated it at 35 per cent. Lindset estimates it at 50 per cent. For Pemberton it is 54 per cent. According to Newman, a third or at least a half of the cases of rheumatoid arthritis must be considered as due to a focus of septic infection. The percentage must be taken as even higher in cases of osteo-arthritis. According to Billinger, Coleman and Hibbs, the claim is made that out of 411 patients studied, 386 cases were due to focal infection. According to Buckley, at least 95 per cent. of the cases are of focal infection origin. According to Wilcox, the gonococcus is the cause of chronic arthritis in only 5 per cent. of the cases, and all the others are due to a process of focal infection.

The focus of infection may be localized in any part of the body. The most frequent localization is in the tonsils, the teeth, the pharynx, and the maxillary sinus either in the frontal or sphenoidal cavity. These deserve very specially to be thought of and must never be forgotten when the diagnostic examination is being made. After these sources come the prostate, the seminal vesicles, the appendix, the stomach, the intestines, the gall-bladder, the fallopian tubes and the peritoneum. Intestinal infection is particularly frequent though it very frequently proves to be the consequence of dental or pharyngeal lesions that prove foci or breeding places of infection. The English clinicians are inclined to think that they discover it whenever they find the streptococcus present in the fecal material. According to Rutch, there is question in these cases of a streptococcus which occurs in long chains and which normally is not present in the intestinal contents. More exceptionally the initial inflammation or focus of infection may reside in ulcerative lesions of the skin.

It is clear, then, that the point of departure of the infection may be situated in practically any part of the body. In clinical practice, however, it is in the teeth and the tonsils that the focus of infection is observed to occur most commonly and it is in these particularly that it is important to look for them.

According to Wilcox, the point of departure for the infection is situated ten times out of one hundred in the tonsil region. In thirteen out of every hundred cases it is in the intestines, and in seventy-two out of one hundred cases in the teeth. According to Buckley, 95 per cent. of the cases are of bucco-pharyngeal origin, that is, they come from either teeth or tonsils. The teeth and the gums must be considered, then, by far the most frequent source of the infection. Nevertheless, Lillie and Lyons consider that the tonsils are responsible for arthritises in at least 79 per cent. of the cases. Pemberton, in a series of 400 cases, estimated that the principal focus of infection was situated in the tonsils in 52 per cent. of the cases, and in the teeth and gums in 35 per cent. According to Cecil and Archer, teeth and tonsils were found to be the cause in 94 per cent. of the cases examined, the tonsils being responsible in 61 per cent. of the cases and the teeth in 33 per cent. of the cases.

The most frequent dental lesion likely to be followed by rheumatismal manifestations consists in granulomata at the apices of the teeth and in an alveolar dental pyorrhea. But there may also be question of pulpitis of the teeth or of apical abscesses, that is, collections of pus at the ends of the roots, or of badly fitting artificial teeth, or of capped teeth where the source of the infection may be hidden under the gold capsule. From this it becomes very clear that it is all-important to practice systematically radiography of the teeth and of the sinuses, but even this may not prove to be sufficient for diagnostic and etiologic purposes. The apex of the root of a tooth may give cultures of virulent microbes even when one cannot observe any microscopic lesions. The focus of infection may actually be situated in jaws from which the teeth have been removed. In nearly 300 cases, Fustermann found in about 130 patients, that is to say, in 45 per cent., a persistent root or a small focus of sepsis in the gum after removal of a tooth to which he did not hesitate to attribute the rheumatism.

Timbrell Fischer contrasts the consequences of pyorrhea and of apical infections. Pyorrhea has a very definite tendency to drain itself into the buccal cavity and to find its way from there down into the digestive tract where it may become not infrequently the generator of acholia, that is, biliary disturbances which lessen the

amount of bile manufactures or secondary infection of the intestines or of the gall-bladder or appendix. On the other hand, apical infections of the teeth have a definite tendency to pass directly into the general circulation and therefore to affect the normal tissues.

While the interest in focal infections has been growing and spreading throughout the medical world, there have been certain discordant voices raised and objections heard. For instance, Burray-Ray does not hesitate to write that "the rôle played by infections of the teeth as the source of focal infection has unfortunately been utterly exaggerated." The extraction in numbers of the teeth made without discrimination in all those complaining of rheumatic symptoms is superfluous and useless. A large number of these infections called apical are strictly shut up and from the practical point of view are not the source of any absorption. As long ago as 1921 Llewellyn Jones launched a rather severe criticism of the doctrine of the buccal origin of rheumatism. Gudzent, in his recent book, says that he had the tonsils removed from a large number of sufferers from rheumatic conditions and the results have not responded to his expectations. In twenty-four patients examined with the greatest care who presented rheumatic manifestations and at the same time a purulent angina, consequent upon infection from the tonsils, only five obtained any relief from the removal of the tonsils. In these cases there was question of patients with sub-febrile conditions and sub-acute rheumatism and purulent foci were definitely found in the tonsils. Gudzent did not obtain favorable results in his patients suffering from chronic polyarthritis, whether progressive or stationary, if they were evolving without fever and without tendencies to sub-acute crises from time to time.

Holsti declares that in the healthy individual the tonsils are regularly and normally in a certain way the seat of slight chronic inflammation. According to him, while angina or tonsillar inflammation may precede acute rheumatic conditions in over 70 per cent. of the cases, it does not precede the relapsing sub-acute rheumatism in even 50 per cent. of the cases and the chronic rheumatism in only slightly more than 22 per cent. On the other hand, the tonsillar infection persists in general after the articular process is cured while only rarely does it happen that the cure of the tonsillitis clears

up the rheumatism. Holsti is inclined to say that there is no connection between the tonsil inflammation and the articular infective process. The ulcerative inflammation of the tonsils is only one of the symptoms of the articular affection whether it is acute, relapsing or chronic.

Tamberg remarks that in his statistics, which include seventy-six cases of acute rheumatism, sixty-three of secondary rheumatism and 257 of chronic, primitive polyarthritises, 79 per cent. of the patients were women. Besides, the age of the patients is not a matter of indifference, for Tamberg, like Charcot years ago, finds that there are two maxima of rheumatic manifestations. One of these is between twenty and thirty years of age and the other is between forty and fifty. He emphasizes the fact that statistics such as these are not favorable to the notion of infection.

Cassidy considers rheumatic arthritis as a clinical entity, a special disease by itself which belongs especially to women. They are likely to be attacked with it in the critical periods of their lives. It is not common, he says, to find a septic focus in these cases. The joint fluids are sterile, as he has demonstrated in a number of patients, by removing fragments of their synovial membranes during life. In but one case out of fifty was he able to find a streptococcus although his cultures were always made with the definite purpose of finding anaërobic as well as aërobic microbes. He thinks that in this case there was a contamination from the skin. Cassidy does not believe that rheumatic arthritis is of infectious origin but believes that it is the result of metabolic disturbances of one kind or another.

According to Llewellyn Jones, rheumatoid arthritis also is not of infectious origin. Its frequency is in direct ratio in the different countries with the occurrence of endemic and exophthalmic goiter. He insists on the frequency among his patients of vaso-motor troubles similar to those which occur in Raynaud's disease.

After this review of the many different opinions held by workers on the subject as to the multiplicity of causes of rheumatismal manifestations, my own opinion with regard to rheumatic etiology will not be misunderstood. I feel that in the immense majority of cases, rheumatism occurs as a consequence of other causes besides infection and in the immense majority of cases it is connected with distrophic and endocrine disturbances. Nevertheless, the existence of arthritises

due to focal infection cannot be denied. The explicit and complete observations of these cases are rare, ever so much rarer than would be usually thought.

The most typical of these observations are as follows:

Rousseau-Decelle reports an observation on a patient suffering from chronic rheumatism in whom the extraction of certain carious teeth was followed at once by a cure.

Jean Croisier has published a clinical observation on a woman of fifty-seven in whom rheumatic crises occurred almost always after a séance with her dentist, whether for extraction or the filling of teeth, or else her rheumatic conditions developed parallel with a dental abscess which terminated by an evacuation of pus.

Santon and Debertrant reported a good while ago an observation on a male patient who presented one after the other an ulceration of the submaxillary followed by multiple arthritis, both conditions yielding at once to an incision which evacuated the purulent collection.

Billings has published an observation on five patients in whom treatment of the pharynx and the teeth brought about the cure of rheumatism which had proved indifferent to all other modes of treatment.

Maranon reports an observation on a patient who was scarcely able to move because of serious arthritic conditions in the knee and the spine and was able to walk without difficulty eight days after a dental treatment. According to Maranon it is always important to think of rheumatism as of dental origin whenever there are suppurative dental lesions, and the patient shows a tendency to a definite relationship between the course of his articular symptoms and those of his teeth. One notes often in such cases febrile crises sometimes premonitory, and there is the appearance of an infectious condition.

Thesee reports an observation on a patient in whom rheumatismal crises appeared when a purulent flow from the teeth dried up. When the purulent secretion was reëstablished once more, the articular symptoms disappeared.

Duclos gives a clinical observation on a patient who presented for a long time repeated attacks of lumbago that proved rebellious to all therapeutic treatment and in whom the definite cure, for he

has not had a symptom for nine years, followed the curettage of a bony periapical focus after the extraction of an infected tooth.

I myself have had the opportunity to see during these late years a certain number of cases of rheumatism undoubtedly, beyond all discussion, of focal origin. In a number of these cases there was question of dental foci as the origin of the infection.

I recall that in a man of fifty years who came to consult me for serious rheumatism which had come on suddenly two months before, accompanied by acute symptoms, and who had, as the result of the affection, become incapable of all work, the only cause that could be found for his rheumatism was a dental infection and the extraction of his teeth cured the man almost as if by enchantment.

With Weissmann, Netter and Oumansky, I reported to the medical society of the Paris hospitals our clinical observation on a woman of forty-eight who had been studied for a long time in the service of Professor Bezancon and who was cured almost instantly by the extraction of her affected teeth.

Quite recently I had under observation a man of some forty years of age who presented for several months an acute condition recalling what is known as Bouillaud's disease. Salicylate of soda was given in doses of twelve to sixteen grams a day, which gave only minimum relief. A suspected tooth was discovered as the result of a systematic examination but it did not seem as though it could be responsible for the condition. Fifteen days later there was a crisis of peri-dental suppuration which necessitated an immediate extraction of the tooth and this was followed by immediate attenuation of the symptoms and then by the cure of the articular phenomena.

In another case in a woman of some sixty years of age who became the victim of a critical period of generalized rheumatism which gradually became worse and worse until finally after two months it held her almost absolutely immobilized in bed, the extraction of some old infected roots brought about an almost immediate arrest of the painful manifestations and was the point of departure for her rapid return to health.

These few observations, among many others, show the intense interest of this question.

Undoubtedly, one should not attribute to dental infection an etiological rôle beyond that which it actually possesses. When rheumatic manifestations occur, it would be a serious mistake to look always to the teeth as the cause of the rheumatism, and it is foolishness, as unfortunately physicians do in certain countries, systematically to remove the teeth of all those who suffer from rheumatism. It is just as important, however, not to fall into this ditch and yet to avoid the opposite danger. It is a serious mistake not to think systematically of dental infection in every case of rheumatism. The failure to recognize this cause as frequently as should be done leads every day to serious therapeutic errors.

Postgraduate Lectures*

TREATMENT OF CARDIAC DISEASES

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HEART-FAILURE WITH PAIN

THIS includes Heberden's angina pectoris and acute coronary artery occlusion. The latter is founded upon a definite pathologic basis; the former is a clinical syndrome, with rather definite features in which several causative factors may operate to produce an attack. These factors may reside in the aorta, in the coronary arteries, in the myocardium, and in the nervous system. Transient anoxemia of some part of the cardiac muscle is probably nearer the underlying cause than disease of any one structure.[1] Differentiation of the two conditions is essential for prognosis and treatment. The following table, taken from East and Bain,[2] is helpful.

	Angina Pectoris	Cardiac Infarction
Onset	During exertion	Often during rest or sleep
Site of pain	Sternum	Sternum
Attitude	Immobile	Restive; may walk about
Duration	Minutes	Hours or days
Shock	Absent	Present
Dyspnea	Absent	Usually severe
Vomiting	Rare	Common
Sweating	Slight	Severe
Pulse	Unchanged	Feeble; often rapid
Temperature	Unchanged	Fever afterwards
Blood-pressure	Unchanged or raised	Lowered
Congestive failure	Absent	Often follows
Heart-sounds	Unchanged	Gallop rhythm or pericardial friction may appear
Leukocytosis	Absent	May be present
Electrocardiogram	May be abnormal	Often diagnostic change
Action of nitrites	Often relief	No relief

The treatment of angina pectoris falls under two headings: that of the attack, and that of prevention.

(1) The patient should carry in his pocket a closely stoppered vial containing 1/100 of a grain nitroglycerin tablets; often 1/50th of a grain is preferable. On the first sign of pain, one of these may ·be slipped under the tongue, and they may be repeated until the pain is eased. The limit is the fulness in the head, which they produce in the susceptible. They should be freshly made every month or so; or else hypodermic tablets may be used by the mouth. They usually are kept more tightly corked than the ordinary preparation taken from the pharmacists' shelves.

Amyl nitrite is also efficacious. It has the objection of smell, which reveals to everyone around the patient his condition, because its odor has become well known. Also sometimes in hypertensive cases, after the preliminary lowering by the amyl nitrite, as the effect wears off the secondary rise of pressure is greater than it was originally. If a more lasting effect on the pressure is desired, sodium nitrite in grain doses every third or fourth hour is preferable.

Hot drinks, especially those containing whisky or brandy, are helpful. Heat to the precordium, in the shape of a hot-water bag or an electric pad, often gives relief.

If the attack is severe, morphine sulphate may be given by hypodermic, 1/4 grain. With the first dose atropine, 1/150 to 1/100 of a grain, would probably add to its efficacy. Beyond that, it may add to the distress by drying the mouth. If a physician or trained nurse is not at hand to give the medicines at once by hypodermic, at least a relative should know the gravity of the situation and be instructed to give them by mouth. Among the newer remedies are papaverine and angioxyl. Papaverine, another alkaloid of opium, in doses of 1/2 grain, has been used by mouth or by hypodermic to relieve attacks, because experimentally it has been shown to have a sedative effect on vascular spasm. Under the name of troparin, a combination of novatropin and papaverine, it is used on the Continent. Angioxyl, an extract from the pancreas which is entirely free from insulin, has a hypotensor effect on the blood-pressure which is not due to any traces of cholin or histamin. It has been tried out in the Vaquez Clinic with great satisfaction. For immediate effect the angioxyl ampoules, two cubic centimeters, should be in-

jected intramuscularly; and to prolong the effect the syrup of angioxyl in one- or two-teaspoonful doses is given in the interval between the injections. It is worth trying in obstinate angina pectoris, especially where there is high blood-pressure. It is claimed that it has not only an influence upon the pressure, but also a trophic influence on the vessel walls as well.

When the attack is severe, oxygen inhalations may be used. Digitalis and strophanthin are useful only where failure of congestion begins to appear, as is shown by incipient pulmonary edema.

(2) Among preventive measures, rest in bed for some days or weeks should be enforced in those cases where the attacks run close together. It is recognized that these painful attacks often run in cycles. When about, the patient should be advised to limit his exertion. His activities should be short of that which induces pain; this, of course, varies with the individual. In walking, the patient should always begin very slowly and gradually increase his gait. By doing this he may be able to go distances with comfort that would be impossible if he hurried at the start. As these patients are apprehensive, their mental attitude must be taken into account. Inform the patient that not all cases of angina are deadly; we all have patients on the list who have had recurring attacks for ten years or more. Often at the beginning the pain is a danger signal for restriction of activity, mental as well as physical, which, if obeyed, may lead to long years of life.

Proper rest at night is essential for these patients. Continuous physical, mental and emotional tensions are bad for them.

The predisposing causes to attacks are over-exertion, excitement, worry, chilling, constipation, dyspepsia, late suppers, large meals and foods favoring flatulence. The diet recommended by F. M. Smith,[8] to be discussed later, may find a place in some of these patients. Small meals, especially at night, and rest immediately after eating, are advisable. Forced dieting, like reduction cures, is not advisable. These patients ordinarily stand eliminating baths rather poorly, though they often do well at Spas, with oxygen, carbon dioxogen and electric baths, carefully supervised. The change of surroundings, the absence of the every-day duties, and the interest in the regimen are probably contributing factors. Such patients with hypertension are ordinarily better off at an altitude of not over three

thousand feet. However, when better, it need not restrict their travel if they remain quietly in their seat or berth when they are at high altitudes. Hypertensive patients frequently recross the continent without any disturbance when they observe this rule. Tobacco should be kept to a minimum. Toxins from focal infections are often provocative factors; so teeth, tonsils, sinuses, gall-bladder, and the prostate must be considered, and, if diseased, the possibility of their correction must be weighed in each particular case.

The presence of syphilis in cases of well-developed angina pectoris calls for the use of mercury and iodides for some weeks. Especially in syphilis of the aorta, neosalvarsan should not be used until the severe attacks have entirely ceased. Postmortem examinations sometimes show structural changes about the mouth of the coronary arteries in this condition, and their rapid destruction by the arsenical compounds are not desirable, especially when acute attacks are going on.

It must not be forgotten that anemia and pernicious anemia, as well as slight hyperthyroidism, are conducive to attacks. When attacks recur, and there is some continuous distress, combined with general nervousness, the use of bromides with chloral hydrate, one to three grains of the latter three or four times a day, as advised by MacKenzie years ago, often makes the patient comfortable. This is a time for a prolonged rest in bed.

The *barbaturic acid series* are useful, because they also allay the nervousness and hyperalgesia in these cases. They include veronal, barbital, luminal, phanodorm, ipral and amytal. There are two methods of using them. One is to give the ordinary dose at bedtime, so as to insure sleep; and with many people the hold-over the next day relieves their distress. Again, it has long been a practice by many physicians to give small doses of one of these preparations, say from 1/10 to 1/5 of a grain three times a day. The *xanthin series* have gained a reputation as diuretics, but some of them also have a great influence in increasing the coronary circulation. Caffeine, in the form of caffeine sodium benzoate, hypodermatically, is good in acute failure; but for constant use the doses necessary make it too much of a nervous stimulant. Theophyllin ethylendiamin,*

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* Theophyldine is the trade name of the American made theophyllin ethylendiamin.

which is the same as euphylline and metaphylline, was shown by Smith to have the greatest influence in increasing the coronary circulation. Theobromin sodium salicylate, diuretin, theobromin calcium salicylate (theocalcin), and theominal, a combination of theobromin and luminal, are useful, but probably less active than the methaphyllin. A five-grain suppository of metaphyllin, used at night, can be tried. Sometimes this is combined with codein. The large doses advised may be more efficacious, but they are apt to upset the stomach. Two to three grains of any of these in capsules three times a day usually can be used for some time with advantage, especially if combined with 1/10 or 1/8 of a grain of luminal.

When there is nervous hypertension, sodium sulphocyanate has been recommended. Bismuth subnitrate in five- to ten-grain doses three times a day is supposed to liberate slowly nitrite radicals which have a desirable effect on the pressure. It may be reiterated that digitalis and allied drugs find their use only when there is beginning cardiac failure by congestion. Later violet rays and diathermy apparently have but a limited use. However, the heat generated by diathermy may dilate the vessels in the area affected and thus reduce the pressure. Sympathectomy is so complicated as compared to paravertebral injections of alcohol, that one would expect to see the injections supplant the operation. In skilled hands, the injection, as performed by Swetlow,[8] is simple, easily repeated, so far as I know harmless, and apparently as efficacious as operation.

TREATMENT OF ACUTE CORONARY THROMBOSIS

In a well-developed case of acute coronary thrombosis, the pain is so overwhelming that nitroglycerin and amyl nitrite are useless. Morphine, always subcutaneously and not less than quarter-grain doses, repeated in a short period, even up to one grain, is the most important procedure. In some cases the pain is so intense, that it is comparable only to the pain of kidney colic, and its very severity seems to be antidotal to morphine. However, the respirations should be watched, and when they tend to become too slow, we must be more careful in the use of the large doses. Even large doses sometimes fail, and ether anesthesia may be necessary. The patient is in shock, perspiring freely, so that he must be surrounded by hot-water bottles or electric pads.

Levine[4] has formulated the best rules we have for treatment. He believes that if the blood-pressure is 100 or over, it is better to avoid stimulation; but if the pulse is absolutely, or almost, imperceptible, caffeine sodium benzoate, even up to one-half or one gram, subcutaneously may be necessary. Also strophanthin and adrenalin intramuscularly may be needed. During the first day the dislodgement of an embolus from the thrombus in the ventricle, or rupture of the ventricle, are less apt to occur than later. This is why early stimulation, where indicated, is admissible; but after the first day or two it is inadvisable. Early digitalis is to be avoided, because it is a question as to whether it can accomplish anything. Furthermore, acute heart-block and ventricular tachycardia are rather common complications in acute coronary thrombosis, and they are probably more apt to occur in a digitalized heart; so that early, if there is edema of the lungs, respiratory distress and cyanosis, the oxygen-tent is the best treatment; but if there is congestive failure, after the first two weeks, when there is less danger of embolus formation, then digitalize the patient, especially if there is auricular fibrillation. If complete heart-block, with attacks of syncope occurring, try first of all the intramuscular adrenalin injections. If they run into the persistent Stokes-Adams syndrome, barium chloride in doses of one-half grain, three or four times a day, may be tried. Attacks of auricular fibrillation, short or persistent, and auricular tachycardia are not uncommon. Levine has seen ventricular tachycardia occur where the conditions seemed most desperate, the pulse jumping to 200 and persisting for seventy-two hours, and yet the patient recovered under massive doses of quinidin sulphate, as much as 1.5 grams five times a day. Naturally, such dosage is to be used only in desperate conditions. There is no condition where relaxation of mind and body is more important than in this condition. For the first twenty-four or forty-eight hours after the attack the bowels may be neglected, unless there is gas or distress. First of all they may be relieved by enemata, followed later by a laxative; but caution against straining should be enforced. A milk diet is the best form early. One of the most important points in the whole treatment is the fact that the patient must be advised to *stay in bed* from *six to eight weeks*, keeping in mind the pathology of the disease; that is, that there is a thrombus sticking to the wall of the left

ventricle, and possibly also extending into the right, if the septum is involved; also that there is a weakened ventricular wall due to infarction makes us realize that to avoid embolism and rupture of the heart, this period of complete rest is quite worth while, as it may mean the difference between recovery or death.

After an attack of coronary thrombosis the patient is naturally anxious, and with reason; but experience has shown that we all have patients on the list who have had typical attacks and yet have been back at their work in from one to four years. A physician, still active, tells me that he had his initial attack nine years ago.

TREATMENT OF HEART-FAILURE WITH CONGESTION

Circulatory failure with congestion suggests at once venous engorgement, dyspnea, cyanosis and edema. This may be central; that is, cardiac, or it may be peripheral, as in shock. The primary factor in cardiac failure by congestion is an inefficient heart muscle which leads to a slowing of the velocity and volume of the blood-flow. Congestive circulatory failure points at once to the digitalis group, but we will defer discussing them until later for two reasons. First of all, they require a section in themselves, and secondly, the profession has been too prone to give digitalis once the diagnosis of cardiac trouble is made. So we will take dyspnea, cyanosis and edema in order.

Dyspnea.—Dyspnea is an early and constant sign of heart-failure. Early it appears only on exertion; later it becomes constant, and finally it may take the form of orthopnea. Then the breathing is rapid and shallow, and is coupled with fatiguing voluntary muscle respiratory movements. This dyspnea of cardiac failure is probably due to an inefficient amount of blood reaching the respiratory center. The quality of the blood may be normal, but the quantity is diminished. This anoxemia constantly stimulates the respiratory center, leading to cardiac dyspnea. Furthermore, the rapid, shallow breathing depends on a reduction in the vital capacity of the lungs, due to congestion of the pulmonary vessels and the consequent loss of elasticity in the lung tissue. The upright position assumed by patients with cardiac failure is known as *orthopnea,* and it is helpful to consider the reasons why a patient assumes this position. If we did this, as doctors, we would be less apt to try to force them to

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bed. In orthopnea we are facing acute failure with high venous pressure and a right ventricle doing its maximum. Field and Bock[5] found that the rate of blood-flow was diminished by one-quarter when the patient was in a sitting position, and by one-half when he was standing. In the upright position, then, it seems that a good portion of the blood is in the dependent parts of the body and the venous return to the heart is smaller. Under these circumstances the output from the right ventricle would decrease, and the left ventricle would be better able to deal with the pulmonary congestion because the left ventricle must pass on the amount of blood delivered to it by the right ventricle if the circulation is to be maintained. Again, it was found that vital capacity is less in the recumbent position than when the patient is upright. In the recumbent position the expansion of the lungs is not complete, because of the upward pressure of the abdominal contents. This is especially true if the liver is enlarged. Use of the accessory muscles of respiration is necessary in this condition, and they can be used satisfactorily only in the upright position. Again, to expand the lungs to the greatest degree the spine must be straight, and this cannot be maintained in a supine position. We know that this type of case is better at rest, but we unfortunately overlook the difficulties they have in attempting to lie down. When the failure is marked, to move them without effort on their own part is not always easy with the ordinary bed. The Fowler bed, commonly found in hospitals, is advantageous, because the back-rest can be brought to any angle by mechanical means, and the lower half of the bed can be elevated mechanically under the knees, which prevents the patient from slipping down. The best bed for cardiac patients is that described by Lewis.[6] The back-rest and the thigh-rest in this bed are also raised mechanically, but in addition there is also a leg-rest and foot-rest; and, furthermore, the whole thing can be easily transformed into a chair, so that the patient can be moved from a recumbent to an upright position without any effort on his part.

In addition to the ordinary dyspnea there may also be paroxysmal attacks in cardiac disease. We refer to those cardiac cases free from acidosis. Sometimes these attacks accompany paroxysms of fibrillation or tachycardia. Occasionally the paroxysmal dyspnea without pain is a sign of coronary thrombosis. Commoner forms ·

of paroxysmal dyspnea are *cardiac asthma* and *acute pulmonary edema.* They are to be expected where the left ventricle is hypertrophied and laboring as in aortic incompetence and hypertension with or without nephritis. The patient is wakened from sleep with a feeling of suffocation and a feeling of impending dissolution. If the attack is short there are a few moist rales in the chest and he may cough up a little thick mucus, sometimes a little blood-stained; but if the attack is long it passes into acute pulmonary edema. However, the latter may arise independently. They both have the same origin —an over-worked left ventricle. In acute pulmonary edema the characteristic thing is the constant cough with profuse pink and frothy expectoration and a chest full of bubbling rales. In both of these conditions morphine is a life-saver. One-quarter of a grain should be injected as soon as the diagnosis is made. In either atropine should be given, 1/100 to 1/50 of a grain with the morphine. In cardiac asthma it may help to prevent the development of acute pulmonary edema, and in the latter it is surely needed. It may be necessary to repeat the dose in short order. If no relief is obtained in perhaps an hour by the injection of morphine and atropine, venesection must be carefully considered. However, the relief is apt to be short, because in pulmonary edema it is the left ventricle that is overtaxed. Where the dyspnea is not so acute, it is still necessary that mental rest and sleep be secured, for they are as important as physical rest. These patients usually are worn by the lack of sleep and by the fatigue of conscious breathing, so that an active drug such as morphine is important. Both in failure by pain and in failure by congestion the administration of ¼ grain of morphine for several days is an excellent manner of building up cardiac reserve. Where the conditions are not so acute, the ordinary hypnotics of the barbital series are enough. They will overcome insomnia, but are not very effective when there is marked cardiac dyspnea. Ammonium or sodium bromide in doses of fifteen or twenty grains three times a day are valuable, as they secure a continuous sedation which the patient needs.

Venesection.—Since already mentioned, it may be discussed here. It is usually more efficacious in the back pressure failure of the right heart in acute infections or emphysema; but it may give temporary relief where the left heart is at fault. When the jugular

veins are distended and tense with blood, venesection should do good.
In this condition the right side of the heart will be found much
enlarged by percussion. The method of choice is the sudden with-
drawal of from 200 to 500 cubic centimeters of blood from the veins
at the elbow. The coarse needle is the easiest way of bleeding.
The old method of opening the vein with a lancet insures a quick
spurt of blood, and often seems to give greater relief. Venous pres-
sure always falls after venesection and remains low if the heart re-
sponds. Gordon took radiograms before and after venesection and
found that there was a reduction in the transverse diameter of the
heart up to 2.5 centimeters in those who responded well; while in
those who did not improve it remained unchanged. It is interesting
to find that blood donors with normal hearts showed no change after
they were bled.

Cyanosis.—Cyanosis is of more importance in diagnosis and
prognosis than in treatment. However, its presence or disappearance
may suggest the success or failure of treatment. In cardiac disease
three reasons for its existence are suggested. It shows, *first,* a
slowed blood-flow because of myocardial failure; *second,* an incom-
plete oxygenation of blood in the lungs, showing that they are either
congested or the site of some pulmonary disorder; and, *thirdly,* it
may point to congenital malformations. In congenital heart-disease
it is due to a left shunt so that venous blood from the right side is
mixed with the arterial blood in the left. This suggests a rather
large defect either in intra-auricular or the intraventricular septum.

Edema.—Edema is the most objective sign of heart-failure that
we have. Cardiac edema is attributed to the slowing of the periph-
al circulation due to an inefficient myocardium. Where the normal
velocity of the blood-flow is reduced by one-half, edema appears.
The slowing of the blood-stream seems to upset the equilibrium
between the capillary and its surrounding tissue-spaces. Cardiac
edema is first found in the dependent parts.

Diet.—When dropsy is present the fluid intake should be re-
stricted and salt should be altogether excluded. The Eka salt, put
upon the market by Sharpe and Dohne,[7] contains no sodium chloride
and seems to satisfy patients. Where the edema is large and the
kidneys sound, the liquid may be reduced to 800 cubic centimeters
or less, but if the kidneys show any evidence of irritation, 1,200

cubic centimeters would probably be better.   Small meals every two or three hours are better than larger amounts.   Orange-juice, milk, cream, jello, junket, carbohydrate gruels and egg-nog may be allowed.   Glucose intravenously improves the nutrition of the myocardium, and by this method it reaches the heart quickly; by the mouth it acts well, but takes longer.   Occasionally in heart-failure acidosis is present, the ketone bodies being derived from faulty oxidation of fats when sufficient carbohydrates are not present.   The presence of ketone bodies in the urine suggests the free use of glucose.   From one-half to two ounces of glucose in lemon- or orange-juice may be used with advantage, and especially in this condition intravenous injections are indicated.

Especially in the arteriosclerotic type of cardiac failure, because of coronary inefficacy, F. M. Smith[8] has found diet and theophyllin of great advantage.   These patients are apt to have gastro-intestinal disturbances, so that the heart shares in the general under-nutrition of the body.   He suggests milk and carbohydrates, especially those easily assimilated, as a major part of the diet.   He begins with 2,100 calories in the form of milk, cream, butter, eggs, puréed vegetables, fruit and cooked cereals.   Dextrin-maltose, dextrose and lactose may be added to increase the carbohydrates.   When edema is present, he limits the fluid intake to 1,500 cubic centimeters, and the salt to a minimum.   On the third or fourth day jellies, salt-free crackers, toast and stick candy are added.   Later, in favorable conditions, additional puréed vegetables and fruit are added, and he gradually changes the food from a soft to a light diet.   In greatly under-nourished individuals, when the excess of fluid is eliminated, the diet is increased to 3,000 calories, which may help promote restoration of cardiac function.   In some cases dextrose solution was given intravenously.   Recovery of the heart has been attributed to the easily available energy provided by the carbohydrates, particularly the sugars.   The liver deranged by chronic congestion may be favorably influenced by the carbohydrates, and thus add to the effectiveness of the diet.   He combines the use of theophylline continually, not only as a diuretic, but keeps it up after edema has ceased because it increases the coronary flow.   This type of treatment does not act so well in the rheumatic type of heart-disease.

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Diet.—When dropsy is present the fluid intake should be restricted and salt should be altogether excluded. The Eka salt, put upon the market by Sharpe and Dohne,[7] contains no sodium chloride and seems to satisfy patients. Where the edema is large and the kidneys sound, the liquid may be reduced to 800 cubic centimeters or less, but if the kidneys show any evidence of irritation, 1,200

cubic centimeters would probably be better. Small meals every two or three hours are better than larger amounts. Orange-juice, milk, cream, jello, junket, carbohydrate gruels and egg-nog may be allowed. Glucose intravenously improves the nutrition of the myocardium, and by this method it reaches the heart quickly; by the mouth it acts well, but takes longer. Occasionally in heart-failure acidosis is present, the ketone bodies being derived from faulty oxidation of fats when sufficient carbohydrates are not present. The presence of ketone bodies in the urine suggests the free use of glucose. From one-half to two ounces of glucose in lemon- or orange-juice may be used with advantage, and especially in this condition intravenous injections are indicated.

Especially in the arteriosclerotic type of cardiac failure, because of coronary inefficacy, F. M. Smith[8] has found diet and theophyllin of great advantage. These patients are apt to have gastro-intestinal disturbances, so that the heart shares in the general under-nutrition of the body. He suggests milk and carbohydrates, especially those easily assimilated, as a major part of the diet. He begins with 2,100 calories in the form of milk, cream, butter, eggs, puréed vegetables, fruit and cooked cereals. Dextrin-maltose, dextrose and lactose may be added to increase the carbohydrates. When edema is present, he limits the fluid intake to 1,500 cubic centimeters, and the salt to a minimum. On the third or fourth day jellies, salt-free crackers, toast and stick candy are added. Later, in favorable conditions, additional puréed vegetables and fruit are added, and he gradually changes the food from a soft to a light diet. In greatly under-nourished individuals, when the excess of fluid is eliminated, the diet is increased to 3,000 calories, which may help promote restoration of cardiac function. In some cases dextrose solution was given intravenously. Recovery of the heart has been attributed to the easily available energy provided by the carbohydrates, particularly the sugars. The liver deranged by chronic congestion may be favorably influenced by the carbohydrates, and thus add to the effectiveness of the diet. He combines the use of theophylline continually, not only as a diuretic, but keeps it up after edema has ceased because it increases the coronary flow. This type of treatment does not act so well in the rheumatic type of heart-disease.

Diuretics.—To get rid of the edema diuretic drugs are usually necessary. The so-called xanthin or caffeine group is among the most efficacious, and is used where the limitation of water and salt is not sufficient. In this group we may include the following drugs with their dosage: for use by the mouth, caffeine, the alkaloid, in doses of from three to five grains in capsule is somewhat preferable to the citrate of caffeine. Caffeine sodium benzoate, from three to five grains, is more often used hypodermatically. Theobromine sodium salicylate (diuretin) is useful in five- to ten-grain doses three times a day, and theobromine sodium acetate from three to five grains. Theobromine acetyl salicylate (theacylon) in three- to ten-grain doses may also be used; theophyllin or theocin from three to five grains; euphyllin or metaphyllin (theophylline ethylendiamin) from one and one-half to three grains. For hypodermatic use caffeine sodium benzoate is largely used. Intravenously theophylline ethylendiamin has been used once daily in dosage of 0.5 grams. It is advantageous because it increases the coronary flow by at least one-third, as demonstrated by Smith.[8] Possibly these drugs cause diuresis by increasing the flow and the permeability of the vessels of the glomeruli, so that the latter filter more fluid. Of course, rest and digitalis alone will often rid the patient of the edema, but in certain cases diuretics in addition are necessary. All these drugs in large doses may cause vomiting, but small doses, taken especially immediately after food, are less apt to do so. Where the ordinary diuretics fail, *novasurol* or *salyrgan*, mercurial compounds first introduced for use in syphilis, were found to have distinct diuretic properties. They are given intravenously and intramuscularly in doses of from one-half to two cubic centimeters. Salyrgan should be used because experience shows it to be less toxic than the novasurol. Diuresis begins in three hours, and is usually over in twenty-four hours. Their activity is much enhanced if the patient receives ammonium chloride in water, fifteen grains three times a day, beginning four days before the salyrgan injection. If the patient objects to the taste, the ammonium chlorid can be given in capsule. It is supposed to act by furnishing a surplus of acid radicals in the blood-stream which must be eliminated. The first dose of salyrgan should be small, inasmuch as some people are susceptible to mercurial preparations, and in these they may produce albuminuria or bloody diarrhea.

Never more than one-half centimeter should be used for the first dose, and two centimeters should never be exceeded; and it should not be used more than twice a week. In pure cardiac failure the results are good. Where there is a fibrotic process in the kidney, not as much is to be expected. Calcium chloride in doses of twenty grains four times daily, well diluted, sometimes acts favorably as a diuretic, as it also supplies an excess of acid radicals. Some French writers[9] think that there is a synergism between calcium and digitalis, so that the latter acts better in the presence of the former; also that if a patient is taking calcium at the same time he is taking digitalis, the digitalis is less apt to cause nausea.

When all other diuretics fail, urea has been tried. One may use from one-half to two ounces in twenty-four hours, given in fruit-juices. Large doses in time will produce nausea. In a recent patient who took large amounts the blood-urea-nitrogen was not appreciably increased, and in any case it usually falls immediately when the drug is stopped. However, it is not advisable to use it when there is renal insufficiency. All other diuretics had been worn out, and this one acted for some time, and then the patient was unable to take it because of the nausea and the tendency to vomiting.

Since the patient cannot take exercise, massage is a great help. In edema of the extremities massage promotes venous return, and the nutrition of the tissues improves.

Other Mechanical Means.—A hydrothorax embarrasses a failing heart, and if of any size it should be removed. The removal of fluid in itself promotes diuresis. The same is true of ascites. Where the legs are greatly swollen, Southey's tubes may be inserted with good results. If the patient is in the upright position for some twelve hours before their insertion, the results will be better. Ordinary precautions against sepsis must be taken. Wrapping the legs in large wads of aseptic gauze and cotton to absorb the liquid is less troublesome and more aseptic than using rubber tubes.

Before taking up the question of digitalis, we may consider a few other drugs used in acute cardiac failure. *Adrenalin* causes a general constriction of the arterioles over the body by stimulation of the sympathetic. It drives the blood from the surface into the splanchnic area. The coronary arteries, however, are not constricted, but dilated by adrenalin in all dilutions. Since adrenalin acts upon

the sympathetic nerve endings in the muscle, and not upon the vaso-
motor center in the medulla, it is apt to give results long after the
vasomotor center has ceased to react, either because of want of oxygen
or toxic poisoning. Adrenalin is a distinct cardiac stimulant. It
increases the output of the heart. If given intravenously, it is much
more evanescent. Adrenalin is the best drug in sudden cardiac
arrest, whether this happens during anesthesia or during a Stokes-
Adams attack. If the heart has stopped, intravenous or subcutaneous
injection is useless. Five to fifteen minims should be injected *di-
rectly into the heart*, according to the following method:

Select the fourth left intercostal space, at the upper border of
the fifth rib, close to the sternum. Use iodine. Take a long, thin,
needle, six to ten centimeters in length. Insert as far as the pos-
terior sternal margin, incline slightly in a mesial direction, push in
four to five centimeters. After some blood is aspirated, make
slowly the injection of one cubic centimeter adrenalin. Movements
of needle due to cardiac contractions are favorable. One reaches
the right ventricle by this method. By this site injury of internal
mammary and pleura is avoided. The fine needles largely preclude
injury of coronary vessels or conducting system. In new-born in-
fants three to five drops of a 1:1000 adrenalin solution in one
cubic centimeter of normal salt has been used.

Adrenalin may also be used to prevent the fits of Stokes-Adams
disease. Ten minims given subcutaneously may abolish the attacks
for some hours. When the heart-block is partial, these injections
may increase the pulse-rate; but when the block is complete, they
have little influence. Generally in the treatment of cardiac failure,
except as above specified, adrenalin has no use, because of its causing
great rise in the blood-pressure, and this will increase the load on
the heart.

Formerly we supposed there was great oxygen deficiency in car-
diac failure; but it has been shown that it is the quantity, and not
the quality of the blood supplied the center which leads to dyspnea
and sometimes cyanosis. However, if there is some disturbance of
the lung, such as emphysema or congestion, oxygen may relieve the
patient. The oxygen-tent is by far the most efficient method. How-
ever, oxygen may be administered by a soft rubber catheter, smeared
with a 2 per cent. novocain vaselin ointment and introduced into

the nose. It should reach the posterior part of the nares, but should not touch the pharynx. The oxygen should be passed through a bottle of warm water at the rate of one or two bubbles a second.

We all use strychnine in cardiac failure, not because it has any influence on the heart, but it reacts on the respiratory and vasomotor centers, and causes vasomotor constriction. The heart has but few vasomotor nerves and will be affected but little. The splanchnic area is well equipped with vasomotor nerves and will be greatly influenced. Thus the heart will receive more blood than it did before. For this purpose perhaps 1/20 of a grain is the minimum that should be used. Strychnine has no influence in peripheral failure, because the vasomotor center does not control the capillaries. It is doubtful whether camphor has much influence in combating circulatory failure, but there is no objection to trying it. Ether and ammonia stimulate, but are fugacious. They are also useful carminatives.

When one has combated the acute failure successfully, the patient must remain in bed until all dyspnea, edema and congestion of the lungs have disappeared. His heart-rate should be below 80 for several days before he tries to get up. After recovery he may gradually return to his ordinary diet; but he should learn to take water half an hour before his meals; also to rest after his meals. Massage and resistance movements are of great value in the after-treatment. Following the resistance movements, guarded exercises should be taught.

The *future.* Once having had cardiac failure, it is apt to recur. Indiscretions of the patient can precipitate it. Increase in the pulse-rate, or slight edema of the ankles, or slight dyspnea should be enough to confine him to bed again for a period.

Some Rules for Cardiac Patients:

1. Obtain as much rest as possible, at least ten hours at night and an hour in bed twice daily.

2. Avoid steps as much as possible.

3. Obtain light exercise in the open air by walking slowly and by deep breathing.

4. Follow diet suggested by your physician, eating the heavy meal in the middle of the day. Coffee and tea in moderation.

alcohol.   Tobacco in moderation or total abstinence if your physician advises.

5. Warm tepid bath every day, if possible.

6. The bowels should be kept well open with the laxative your physician prescribes.

DIGITALIS

The effects of digitalis on the heart are:

1. A direct depressant action on the conducting tissues.

2. A stimulation of the vagus, producing:

(a) A slowing of the pace-maker in the S-A node

(b) A shortening of the refractory period of the auricular muscle.

(c) A further lessening of conductivity in the conducting tissues.

3. A direct action on the muscle fibers of the heart, causing an increase in the strength of the systole and a prolongation of the refractory period.

The most profound effects of digitalis are in auricular fibrillation and flutter. This will be considered in detail under the arrhythmias. In at least 70 per cent. of cases of prolonged cardiac failure auricular fibrillation is present. In the remaining cases a normal S-A rhythm is maintained throughout. Parkinson and Clark Kennedy[10] have reported on the type of patient in which a regular rhythm is apt to continue to the end. They found that normal rhythm is likely to persist in acute infections of the heart, like infective endocarditis and acute rheumatic carditis, in aortic incompetence, especially syphilitic, in essential hypertension and in patients with pulmonary lesions, as long-standing asthma, bronchitis and emphysema with their accompanying right ventricular hypertrophy. In these patients with a regular rhythm digitalis does not slow the pulse as it does in those with auricular fibrillation. However, sometimes in children and occasionally in adults it does retard the pulse by its vagal influence. In every case of failure by congestion, though the rhythm is regular, digitalis should be tried, because especially where dropsy is present it often produces diuresis and causes venous congestion to disappear and the liver to recede if it is enlarged. It has very little influence on the blood-pressure. Since we do not have the apex-rate as a guide in the dosage of digitalis in such patients, it is well to esti-

mate the amount of digitalis necessary to saturate the patient and keep well within that dosage. Even though the pulse is not slowed much, the disappearance of dropsy and venous congestion are definite signs of improvement. In these patients we should watch for the first signs of gastro-intestinal disturbances, as nausea, and withdraw the digitalis at that point. The only real contra-indication to digitalis is a partial heart-block, where giving of digitalis increases the block and leads to dropped beats. In these patients it must be used with care. In complete heart-block there is no danger in the use of the drug. It will not affect the ventricular rate, but will strengthen the ventricular systole and may be beneficial in ventricular failure. Where there is cardiac failure digitalis may be tried in branch bundle block, in alternation, in high blood-pressure and even in aortic regurgitation. If extra systoles existed before the administration of digitalis, then the drug does no harm. Digitalis often fails in tachycardia of fevers and hyperthyroidism, in chronic renal disease and in syphilitic aortic valve lesions.

Preparations of Digitalis.—The American Heart Assocation has just recommended that tablets or capsules of powdered digitalis leaves be dispensed in all cases where digitalis is indicated, except in emergencies. They usually come in grains 1.0 or grains 1.5, the former equivalent to ten minims, and the latter to fifteen minims of the tincture. The tincture is a good preparation, but it is not uniformly standardized at present, so that some preparations are under par and others are over-active. For that reason the powdered leaf is recommended. The infusion of digitalis is a good preparation, but it must be fresh, because it rapidly deteriorates, and it has the same objection as the tincture. There are a large number of excellent proprietary remedies. Their only advantage has been their uniformity and sometimes the smallness of bulk. The Nativelle preparations are always uniform. The white granule, grains 1/240, is equivalent to fifteen minims of the tincture; the small red granule, grains 1/600, is equivalent to about six minims of the tincture. They are called "crystalline digitaline," but they probably contain a large amount of digitoxine. There is an ampoule of Nativelle's digitaline in which one cubic centimeter contains 1/300 of a grain, which may be used intravenously. There is another ampoule for intramuscular use, containing grains 1/120. Digitane is an old standby,

alcohol. Tobacco in moderation or total abstinence if your physician advises.

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long used under the name of digipuratum. The Upsher-Smith capsules are excellent, and there are many other very good preparations.

Where quick cardiac stimulation is needed, strophanthine intravenously is preferable. It may produce results in half an hour, or less. If the patient has had digitalis before, a full dose of strophanthin should not be repeated in twenty-four hours. The preparation of choice is Arnaud's ouabaine. It is uniform, quick and effective. They furnish an ampoule containing grains 1/240 of crystallized ouabain for intravenous use. The dose is from 0.5 to one ampoule. Unless the condition is urgent, it is probably better not to repeat for twenty-four hours. There is also an ampoule grain 1/120 of Arnaud's ouabaine meant for intramuscular use, and is so marked. It could be used once or twice in twenty-four hours, but if the patient has been taking digitalis before the effect on the heart must be watched closely.

The Rectal Use of Digitalis.—The absorption from the rectum is rapid and the dosage the same as that given orally. Aqueous preparations are less irritating. The tincture may be diluted with normal saline solution, one part of the tincture to five of saline. A cleansing enema should be used first. Warm the digitalis and introduce slowly through a small catheter. It is especially useful in the cases of splanchnic congestion.

The Physiologic Limit of Digitalis.—The toxic effects of digitalis show themselves by gastro-intestinal irritation and by certain changes in the rhythm of the heart. To insure thorough digitalization we push digitalis to the first signs of gastric symptoms, usually anorexia and possibly nausea. Beyond this it is not desirable to go, for next come vomiting and diarrhea. Vomiting is not due to gastro-intestinal irritation alone, but especially it is of reflex origin due to direct action on the heart ganglia. Too much digitalis produces sinus arrhythmia, sudden slowing, heart-block, extra systoles, ventricular tachycardia, and frequently ventricular fibrillation. Such undesirable effects are apt to occur only if the patient is not asked to return often enough for observation when taking the drug. Atropine tends to overcome the effects if they are disturbing; but digitalis should never be pushed to such a limit. At the first sign of nausea, or in the presence of coupled beats it should be discontinued.

Method of Giving Digitalis.—Although digitalis has been used for 150 years, it is really only since the discovery of auricular fibrillation that we have understood fully its potentialities. All are now agreed that the patient receives greatest benefit from digitalis only when he is saturated with the drug. Again, much has been learned about the standardization of digitalis. The commonly used unit of potency today is the weight in milligrams of the dry drug which is required to kill a cat weighing one kilogram when the solution of the drug is injected slowly into a vein. This is called the "cat unit." One hundred milligrams of a good specimen of the dried leaf is usually taken as one cat unit. Naturally, the amount of digitalis needed to saturate the patient depends upon the size; and it has been found that for full digitalization in man 0.15 of a cat unit per pound of body-weight is required. Eggleston[11] has introduced the following formulae for calculating the amount of digitalis necessary to thoroughly digitalize a patient whose weight is known:

I. $$\frac{C.U. \times 0.15 \times W.}{1000} = \text{grams of powdered leaf in total amount}$$

$$\frac{100 \times 0.15 \times 140}{1000} = 2.10 \text{ grams or about 42 grains}$$

In this formula C.U. refers to cat units, and W. to weight. If a man weighs 140 pounds, including his edema, then the formula will show, when these figures are substituted, that this patient would require for saturation 2.1 grams, or about thirty-two grains of the powdered leaf. If the tincture is to be used, the formula is a little different:

II. $$\frac{C.U. \times 0.15 \times W.}{100} = \text{cubic centimeters of tincture in total}$$

$$\frac{100 \times 0.15 \times 140}{100} = 21 \text{ cubic centimeters or 357 minims (nearly 6 drams)}$$

The second formula, a little different, because the tincture is a 10 per cent. preparation, shows that if the patient weighs 140 pounds he will need twenty-one cubic centimeters or 357 minims, or nearly six drams of the tincture.

The chief value of these formulae is the estimation of the amount of the digitalis preparation necessary for full saturation of the patient, in which condition we get the best results from the drug.

Eggleston has also formulated certain methods of administration.

First, the *small*-dose method. Two to four grains of powdered leaf, or twenty to forty minims of the tincture, are given every six hours until the desired effect is obtained. This method may require as much as ten days. Second, in the *large*-dose method the patient may be digitalized in one or two days; six to seven grains of the powdered leaf, or one dram of the tincture is given every six hours in the first twenty-four hours. In the second twenty-four hours one-half of the original amount is given every six hours for four days, and this last dose and interval continued until the desired effects are obtained. Third, the *body-weight* method was introduced, so that the calculated amount may be given in very large doses in urgent cases. The total amount necessary to digitalize a patient of given weight is estimated by the above formulae. One-third to one-half of this total is given at once; after six hours one-fifth to one-fourth is given; six hours later one-eighth to one-sixth is given. If more is needed, one-tenth is given every six hours.

Certain precautions must be exercised in the large-dose method. It should be ascertained that no digitalis has been given for ten days previously, and the condition should be urgent. If digitalis has been given, the procedure is the same; but three-fourths to one-half of each dose should be used. In giving digitalis it is probably better not to give doses oftener than at intervals of six hours, as it takes this time for full absorption from the stomach. The body-weight method, it seems to me, is entirely a procedure for use in hospitals or where sufficient skilled nursing is available. Otherwise if the condition is urgent, intravenous injections of strophanthin (ouabain), possibly repeated once or twice at two-hour intervals, followed by forty minims of the tincture of digitalis once in six hours is usually sufficient to give good results.

Treatment of the Arrhythmias.—In auricular fibrillation the normal pace-maker is replaced by a circus movement. The impulse revolves at the rate of 400 to 500 times a minute. Fortunately the bundle of His can transmit not more than 200 of these irregular impulses, and the ventricles beat at a correspondingly rapid and irregular rate. Though the rapid clinical rates are from 180 to 160, they lead to heart-failure with diminution of urine output and dropsy. It is in the treatment of auricular fibrillation that digitalis shows its most brilliant results. It affects the circus movement in-

directly through its influence on the vagus, but more important is its depressant action on the bundle of His and through the vagus, so that the number of impulses transmitted to the ventricle is lessened and the ventricular rate is slowed. In full digitalization the slow rate is largely due to an indirect depressant action on the function of the conducting tissues. The slow ventricular rate makes the diastole longer, so the ventricles are better filled, the rest of the heart is increased, and the force of systoles strengthened. · This leads to increased urinary secretion and disappearance of edema. The aim is to reduce the ventricular rate to seventy or eighty per minute. In auricular fibrillation the question of dosage is determined by the rate of the heart at the apex, the degree of heart-failure, and the urgency of the symptoms. The best results are to be expected in the rheumatic group rather than in the arteriosclerotic. However, any patient whose apex-rate exceeds 100 at rest should be given digitalis. Those with slower rates are apt to have less urgent symptoms, and the small-dose method of twenty minims of the tincture every six hours will be sufficient. The total quantity of the tincture needed to saturate the patient can be predetermined by the weight of the individual including his edema. In the individual of average weight this will be around six drams; and as about twenty minims of the tincture are burned up or excreted during the twenty-four hours, full digitalization will probably be attained when the patient is taking seven drams in all. Where the apex-rate is higher and the symptoms more urgent, we may resort to the large-dose method already spoken of under digitalis. If the rate is extremely rapid and the degree of failure marked, I prefer to begin with the intravenous injection of ouabain, grains 1/240. As the patient has usually been taking digitalis, he must be careful about the repetition of the dose, so that one or two in twenty-four hours may be sufficient. In the meantime the digitalis given by mouth will have time in which to take effect. The amorphous strophanthin, which is sometimes the only one available, is good; but is not as active as the ouabain. In using large doses of digitalis or intravenous ouabain, the patient must be kept under observation and the apex-rate checked every four hours. We must realize that the pulse as ordinarily taken in the wards is perfectly useless. Whenever the pulse-rate falls to eighty the digitalis should be reduced. If coupling appears it should be dropped. No bad

effect will result in dropping a dose or so, because digitalis is slow in disappearing. It must be remembered that in febrile cases we should not push digitalis quite so far as in the afebrile. It will be better to be satisfied with a rate of eighty or ninety. There is an occasional patient who cannot take digitalis in any amount without at least gastro-intestinal symptoms. In these patients the tincture of strophanthus may be tried. It deteriorates quickly so that it should not be mixed with water until the patient is just ready to take it. Squill in the form of the tincture or the powdered drug in capsule is useful in these patients; but the dosage must be larger than ordinarily given.

After Treatment.—This is important because the cases that will not need a maintenance dose to keep the pulse slowed are very few. The average case will need ten minims three times a day to maintain an apex-rate of seventy or eighty. If enough digitalis is not given continuously the rate will slowly rise to its former level and the good be undone. This amount is necessary because it maintains the original saturation and effect of the digitalis. Intelligent patients quickly learn the amount necessary to keep the heart at a reasonable rate.

Auricular Fibrillation and Quinidine.—Digitalis controls the rate of the ventricle in fibrillation, but it does not bring the rhythm back to normal. Quinidin may cause a return of normal rhythm. In hyperthyroidism after operation quinidin should be used to secure a normal rhythm when this does not return spontaneously. However, there are certain contra-indications to the use of quinidin. No patient with heart-failure or active infection should be so treated. If fibrillation has not persisted too long, especially in the rheumatic group, the expectations of maintaining a normal rhythm are better.

Action of Quinidine.—It depresses the vagus, lengthens the refractory period and slows the conduction time in the auricle. Thus it always slows the circus movement. The auricular rate under the influence of quinidin may fall from 500 to 200. The direct action of quinidin on the muscle, and the indirect action through the vagus are the same; but the effect upon the gap in each of them is two-fold and "mutually antagonistic." They each prolong the refractory period and slow the conduction time. If the refractory period is affected more than the conduction time, the gap will close and the

circus movement will end. This occurs in 50 per cent. of cases. We have seen that quinidin slows the auricular rate, and the slower the auricular rate the more impulses reach the ventricle. An increase in the ventricular rate is to be expected before normal rhythm is restored.

Preliminary Treatment.—Any heart-failure present should be first treated with rest and digitalis. All signs and symptoms of heart-failure must disappear before quinidin can be used. Many prefer to give a preliminary course of digitalis and not commence quinidin until the ventricular rate is below eighty. Digitalis and quinidin are not given at the same time. A dose of three to five grains of quinidin should be given as a test for susceptibility some hours before the actual treatment is begun. Then quinidin sulphate in five-grain capsules is given every four hours, preferably after food, and one dose should be given during the night, because if the interval between doses is too long the effect is lost. The patient should remain in bed from the beginning of treatment, because as the auricular rate slows the ventricular rate is apt to increase and sometimes becomes very rapid. Occasionally a marked persistent tachycardia, urticaria, headache, dizziness, nausea and diarrhea will bring the treatment to an end. In favorable cases the pulse may become perfectly regular in a few days; but the trouble is that it is not usually long-lasting, the fibrillation being resumed in days, weeks or months. In a small percentage of cases the normal rhythm persists, and in a larger percentage it will persist if the patient is rationed upon small doses of quinidin. Two or three grains two or three times a day have kept certain patients comfortable, and they have taken it indefinitely. In mitral stenosis with auricular fibrillation I have seen embolism occur as frequently without quinidin as with it, although theoretically it should be commoner in the latter instance. Once having had chronic fibrillation, excessive exertion, heavy labor and strenuous games should be avoided. This is particularly true if digitalis is constantly needed to maintain the low ventricular rate; and if breathlessness and precordial distress are easily induced, the patient should eat simply, drink water between meals, spend long nights in bed, and avoid exposure when influenza and epidemic colds are prevalent. The belladonna series, as in cold medicines, are to be avoided, as they tend to increase the heart-rate.

The strain of pregnancy and labor are dangerous to patients with fibrillation. That operations may be carried through successfully where absolutely necessary is suggested by the results in hyperthyroidism. Usually auricular fibrillation is a chronic and persistent complaint, but in certain patients there are transient attacks which may last a few hours or days. In such cases it is probably better not to give digitalis treatment until the condition has lasted at least two weeks. Here quinidin sulphate may have a more desirable effect.

AURICULAR FLUTTER

The best remedy in the treatment of auricular flutter is digitalis. The drug should be given in the usual dosage until the ventricular rate is slowed. At this point an increase in the dosage of digitalis is frequently followed by a change from flutter to fibrillation. At this time if the digitalis is withdrawn the fibrillation often ceases and the normal rhythm is restored. In case fibrillation persists, we should aim to keep the ventricular rate about eighty, and the patient will be more comfortable than he was with flutter. If for any reason the patient cannot take digitalis, we may resort to intravenous use of strophanthin or ouabain, with excellent and often more speedy results. Quinidin sulphate has been used for flutter, but digitalis is preferable. In flutter quinidin slows the auricular rate, and when the rate has reached 200 or less the ventricle may answer to every stimulus, giving us a reaction not to be desired.

HEART-BLOCK

Partial heart-block of sudden onset means an active process. This calls for rest in bed and a thorough search for the cause. Acute infections, especially rheumatic, are often the etiological factors and may be treated on accepted lines. If this mild heart-block remains after treatment, the patient should be repeatedly examined. If there is any indication for digitalis, it may be used. It increases the block, but it may be beneficial and can be administered if the patient is watched carefully. If beats are dropped, atropine may be given, thus eliminating any vagal influence. Advanced heart-block, whether partial or complete, is usually a chronic process. Especially in middle life is syphilis a common cause. Any history or evidence of this complaint means that active treatment should be administered,

usually mixed treatment succeeded by intravenous treatment with arsenical compounds.

The Stokes-Adams syndrome occurs especially where the heart-rate is passing from partial to complete block and *vice versa,* or in complete block where there are sudden and steep falls in rate. These people suffer from spells of unconsciousness and localized convulsions. To prevent convulsions adrenalin 1:1000 solution may be given in ten-minim doses subcutaneously. When the heart has stopped, sub-cutaneous injections are useless. A half cubic centimeter may be injected directly into the heart. Such intracardiac injection usually stimulates contractions at once. For unconsciousness and for repeated fits artificial respiration, oxygen, strophanthin, digitalin and the nitrites have all been used. Atrophine is an old remedy, given intravenously to abolish the attacks. Barium chlorid increases the excitability of the heart-muscle, and may thus aid in avoiding the fits. It may be given by the mouth. The usual dose is 0.5 grains three times a day. Much larger doses are recorded without giving rise to extra systoles or gastro-intestinal irritation. The maximum dose would seem to be one grain three times a day. Ephedrin has been suggested, since its action is like adrenalin. A half grain by mouth three times a day has been recorded as abolishing the fits. This must be taken with some reserve, as the fits may cease spon-taneously. One must bear in mind that ephedrin in such doses, at least after a time, may provoke urinary retention. The general supervision of the patient with respect to digestive disturbances or over-activity, physical or mental, should be borne in mind, as they may tend to provoke fits.

SIMPLE PAROXYSMAL TACHYCARDIA

As preventive measures in those having had attacks, tea, coffee and tobacco should be eliminated. The gastro-intestinal tract should receive special supervision, for flatulence is a frequent determining cause of attacks. Infectious foci should be eliminated. Where the attacks tend to recur, large doses of digitalis daily may ward them off, or in the non-susceptible doses of quinidin sulphate, from two to five grains three or four times a day may be used for some time. For the actual attack nervous stimulation by pressure on the eyeball or vagus in the neck should be tried. Pressure upon the abdomen,

a tight abdominal binder, the doubled-up attitude of the patient, and holding the breath all may affect the process by influencing the venous return to the heart. Since pain, anginal in type, is a common symptom in these patients, morphine and chloral may be necessary to ease the pain and secure sleep. Where cyanosis and venous congestion are extreme, venesection must be considered. For respiratory embarrassment oxygen is useful. An ice-bag over the heart often gives relief. Sometimes quinidin sulphate in five-grain doses four to six times a day will break up an attack, and 0.2 gram intravenously has abolished the attack. Digitalis, strophanthin and ouabain intravenously have all been used. In my own experience quinidin has seemed to be the better drug for both prevention and cure.

Alternation of the heart calls for rest, both physical and mental. Digitalis may help.

PREMATURE BEATS OR EXTRA SYSTOLES

These in themselves are not a sign of myocardial trouble, though they often are associated with myocardial change, the diagnosis of which is based on other findings than the premature beats. They are frequently aggravated by tea, coffee, tobacco, alcohol and gastro-intestinal disturbances in the susceptible. Quinidin sulphate in doses of two to five grains twice or thrice daily will often abolish them. If combined with two or three grains of brometone in the same capsule, the effect is more decisive. Extra systoles do not contra-indicate the use of digitalis except in those patients in whom it has produced this condition. Toxic doses of digitals may cause extra systoles, whereas Wenckabach found that small doses of digitalis cured extra systoles. The premature beats so often come and go that it is only when their presence renders the patient nervous that active treatment is necessary. Perhaps it is more important to abolish the auricular premature beat by the means given, because occasionally one sees such a case ultimately run into auricular fibrillation.

CERTAIN INFECTIONS OF THE HEART

Rheumatic Fever.—We must bear in mind that not only the valves and the endocardium, but that the heart-muscle as well is

affected in rheumatic fever. It is a pancarditis usually that confronts us. Prolonged rest is the major factor in treatment. This should be begun the moment the disease is diagnosed, and should continue until all evidence of the infection has subsided. The heart-rate should be normal, the fever should disappear, and the signs and symptoms should disappear or become stationary. Even after this, further rest for weeks or months is necessary. If the tonsils are diseased, they should be removed during the first quiescent period, if possible. Salicylates ease symptoms, but do not remove the cause. Especial attention should be paid to chilling, to wet feet, exposure to cold and wet, especially in spring when the attacks are more apt to occur. Occasionally when you have a tachycardia in children digitalis will slow the heart, especially by its influence on the vagus. This is not always true. The study of the rheumatic problem should make every doctor a proselytor for convalescent homes, where such patients can have the proper rest for a sufficient length of time, and where it can be done at half the rate that the ordinary hospital costs. We must all grasp the concept that the cure of a heart once infected by rheumatic fever means rest for months rather than days or weeks.

Cardiac Syphilis.—We have long suspected syphilis when there was aortic valve disease and disease of the proximal part of the aorta. To this must be added now a diffuse syphilitic myocarditis affecting the heart-muscle. Formerly there was great skepticism about being able to do much for these patients, and the reason was that little was tried consistently, persistently and early. Once failure by congestion appears there is little chance of doing anything. As soon as the condition is recognized, whether it be in the form of myocarditis or involvement of the aortic valves, iodide of potassium and mercury should be given. After two weeks or more the intravenous use of the arsenicals gives excellent results, provided the beginning dosage is small enough, say 0.25 gram, to be increased by 0.1 gram weekly.

The Heart in Pneumonia.—The routine administration of digitalis in pneumonia is inadvisable. Statistics are accumulating tending to show that the groups without digitalis do better than those with. If the patient has had old cardiac failure, and this tends to recur during pneumonia, then the patient should be digitalized;

and we must bear in mind that it is apt to take larger doses to get an effect when the myocardium is in the grip of a toxemia. In the ordinary case where the heart is sound to begin with, we can wait; and if later in the disease the heart begins to lag, intravenous strophanthin or ouabain will give an effect in a short period; and this can be followed by digitalization. We must remember that cyanosis in pneumonia may be due to peripheral failure and not to cardiac embarrassment. Blood-letting is sometimes necessary; but the oxygen-tent and cold sponging may be more efficacious.

The Heart in Diphtheria.—The most important element next to antitoxin in the treatment of diphtheria is absolute rest. Fortunately we see but few of the old virulent infections that were a common sight years ago, thanks to the early use of the sera. But it is well to bear in mind that every subject with diphtheria is a potential subject for circulatory failure, both cardiac and peripheral. Even in the mild cases if there is any tachycardia, weakening of the heart-sounds, or slight fever persisting, the patient should be kept flat, even after the third and fourth weeks. Otherwise sudden death may occur. It is well to be adamant in your attitude toward the parents and patient in this requirement.

In subacute infective endocarditis rest, forced feeding, fresh air, and plenty of sunlight are of primary importance. The intravenous injection of sodium cacodylate in large doses, as advocated by Capps and Billings, is worth a trial.

THE HEART IN THYROID DISEASE

Excessive or diminished thyroid secretion has a decided effect upon the circulation. Hyperthyroidism leads to tachycardia, later paroxysmal, and finally, in a large percentage of cases, to permanent auricular fibrillation. There are some experimental and pathologic facts suggesting that large amounts of thyroid secretion may cause myocardial degeneration. However, the absolute recovery of many thyro-cardiacs with marked decompensation after thyroidectomy is complete.

The tachycardia in hyperthyroidism is due to sympathetic stimulation and the increased metabolism which calls for a greater systolic output from the heart. Malnutrition, shown by loss of weight, affects the heart as well as the body as a whole. In hyperthyroidism

the pulse-pressure is increased. It suggests the pressure of aortic incompetence. In the thyro-cardiac of long standing, the heart may be enlarged, and it may or may not be associated with valvular defects.

Treatment of the cardiac complications of hyperthyroidism presupposes a recognition of the underlying thyroid disturbance. This is not always an easy matter to decide. Some of the severest thyrocardiacs belong to the group which Lahey calls apathetic hyperthyroidism. The commoner activating group may reveal one or more of the group of symptoms which gives the clue to the diagnosis. The apathetic type is quiet and elusive; and yet, above all, an early diagnosis is important, to avoid the changes which come with time. If the picture is defective, the following, in the order of importance, give a clue.

Increased basal metabolism is highly suggestive, and even when it exists alone, with nothing else to explain it, it is practically diagnostic. The therapeutic response to full doses of iodine is important in diagnosis. The whole clinical effect, and not its effect on basal metabolism alone, should be taken into consideration. Loss of weight, especially with good food intake, is important in diagnosis. Likewise are physical weakness and tremor. Tachycardia, even slight, if persistent, should arouse suspicion. Every case of auricular fibrillation may be scrutinized with advantage. Especially in the exophthalmic variety the gland may be very small.

The treatment, once the diagnosis is made, is surgical. If the patient will not agree at once to do the best thing, then rest should be enforced, sleep secured by hypnotics, or perhaps better by morphine sulphate. Edema should be combated by the usual diuretics. Iodine may be tried as a therapeutic test for a short period, if you are sure you are not dealing with toxic adenoma, but never more than three months in exophthalmic goiter, and not more than one week when there is an adenoma that may be toxic. The use of digitalis in hyperthyroidism is restricted. In the heart disturbed by excessive thyroid secretion alone, digitalis seems to have but little influence in slowing it. In heart-disease due to previous infection, like rheumatic fever, where hyperthyroidism is superimposed, digitalis may act better. In Lahey's clinic they use it in two conditions only—one where rest and iodine have failed to bring about lowering

of rate and improvement in decompensation; the other where the rate remains extremely high. Once having decided that digitalis is needed, it may be necessary to give rather large doses before securing any effect. There is a possibility that the increased combustion going on in the system may destroy digitalis more rapidly than usual.

ANESTHESIA IN HEART-DISEASE

The condition of the myocardium is the important factor. Immediate heart-failure is a contra-indication, and past heart-failure would lead one to think of emergency operations only, or where it is to relieve intolerable pain. The one exception to this rule is hyperthyroidism. In the Lahey Clinic they have operated upon a long list of cardiac patients where heart-failure was overcome, with a very small mortality. They avoid operations within at least three weeks of congestive failure. What appeared to be hopeless auricular fibrillation often disappeared after thyroidectomy, either voluntarily or following the use of quinidin. Of course, there is risk in the operation, but apparently it is a risk worth taking in an otherwise hopeless condition.

In all patients, especially elderly people, one must assess the condition of the heart muscle, its limitations, reserve power, the blood-pressure, and the state of the kidneys in making a decision regarding operation. In acute rheumatic conditions the removal of the tonsils always comes up. When infection is no longer active, they may be removed.

Choice of Anesthetic.—*Ether* is the anesthetic of choice in ordinary heart-disease. It is a cardiac stimulant and acapnia can be prevented with proper methods of administration. In deep anesthesia from ether, Levine found the same arrhythmias may take place as do experimentally. Electrocardiograms taken during anesthesia showed extra systoles and nodal rhythm. The usual dose of atrophine and morphine, given before the anesthesia, tends *to* obviate this disturbance.

Gas and *Oxygen.* Anesthesia with gas alone raises blood-pressure and causes asphyxia. It throws extra work on the left side of the heart. It is not the anesthetic to be selected in cases of high blood-

pressure or in aortic regurgitation. Of course a large part of the undesirable effects of gas is offset by the use of oxygen.

Intraspinal Novocain. Anesthesia is produced with this method by paralysis of the dorsal nerve roots. Paralysis of the sympathetic nerves occur at the same time as the sensory nerves when the anesthetic region reaches about the second lumbar root. A fall of blood-pressure is a prominent feature in spinal anesthesia. This fall of pressure may be so great as to suggest a general vasodilatation, with blood collecting in the dependent parts. However, this fall of pressure does not occur if the effect of the drug can be restricted to the lumbar and sacral roots, especially if the Trendelenberg position is maintained. At the level of the fifth thoracic it causes general splanichdilatation, and if its effects should reach higher there is danger of its involving the phrenic and other respiratory nerves. If cases of low blood-pressure are excluded, and the spinal anesthesia is used only for operations in the lower abdomen, the mortality is negligible. Spinocain is now used. It is a mixture of novocain, ephedrin and strychnin sulphate. The ephedrin is used to prevent the profound fall in pressure. It acts as well as adrenalin and persists longer.

Sudden Cardiac Arrest During Anesthesia.—The *use of adrenalin*: If adrenalin is to be used, it should be used promptly. Probably not more than five minutes should be allowed to elapse if results are to be expected. Adrenalin has been injected both into the veins and also directly into the heart. One cubic centimeter of a 1 :1000 solution is the actual dose. The heart usually starts to beat as soon as the adrenalin reaches it, and the respirations begin shortly afterwards. Artificial respiration should be kept up during the whole time. Sometimes the cerebral anemia leaves after-effects. The patient may be unconscious for some time, and for a much longer time he may experience confusion, dizziness and headaches.

Intracardiac injections are used for syncope, not only in anesthesia but in profuse hemorrhage, traumatic collapse and asphyxia. The method has already been described under "adrenalin."

THE HEART IN PREGNANCY

The treatment of the heart in pregnancy belongs in large part in the domain of preventive medicine. If a woman with heart-

disease asks you about the risks of pregnancy, there are a few general rules, derived from the various lying-in hospitals, that can be applied first of all. Some of them are as follows:

Failure by congestion, recent or past, forbids pregnancy.

Permanent auricular fibrillation, especially if the heart is enlarged, or if it shows an evident lack of reserve power, forbids pregnancy.

Recent rheumatic fever makes pregnancy a great risk.

Aortic insufficiency is the cause of a large maternal mortality.

If coupled also by mitral stenosis, the condition is even more grave.

Mitral stenosis with a diastolic murmur filling diastole is a serious risk.

Because a woman with such a lesion has survived one pregnancy, it does not follow that she will bear a second. Almost always a woman with a mitral obstructive lesion has reduced reserve after the first pregnancy.

Hypertension, especially if there is any sign of kidney involvement, is a contra-indication to pregnancy.

When pregnancy exists, one ought to have some formal rules of prognosis, which should be a guide in determining whether the heart would stand the strain of pregnancy. In 1921, Mackenzie stressed the importance of the limitation of the heart to effort. More than ten years before in his wards, he was wont to say "forget the murmurs and tell me what the heart can do." Pardee[12] bases the prognosis for pregnancy upon the functional cardiac diagnosis, just as in the non-pregnant. His attention is centered upon the ability of the patient to perform physical exercise, rather than upon the pathology of the valves or myocardium. He has formulated the following rules:

Class I. Those who are able to perform ordinary and usual physical activity without unusual fatigue, palpitation or dyspnea.

Class IIa. Those who are able to perform the usual normal physical activity, but who have discomfort in so doing. Such a person would have noticed an increase in the shortness of breath after climbing stairs, or after walking against a wind or up-grade, or after such work as house-cleaning or lifting heavy articles. These patients would by some be designated as fairly well compensated.

Class IIb. Those who are unable to perform the more difficult features of ordinary physical activity without stopping, on account of fatigue, shortness of breath, or palpitation. Such activities would be climbing two flights of stairs, or walking a half-mile at an ordinary rate. These might be called somewhat decompensated.

Class III. Those who are unable to perform the simplest physical activity without fatigue, or shortness of breath, or palpitation. Such patients would be unable to walk 200 or 300 feet, or climb one flight of stairs, without resting, and would be unable to do any housework. They would be said to be much decompensated, or definitely decompensated.

In using the rules, he stresses the necessity of determining that the patient definitely has organic heart-disease, by observing the ease with which unusual shortness of breath or palpitation develops after exercise, and the observation of the patient's reaction to test-exercises given by the physician. Swinging a ten- or, perhaps better, a five-pound dumb-bell from between the legs to straight above the head is his test exercise. The patient should do this twenty to twenty-five times under observation, and the pulse-rate and dyspnea should be noted immediately. There will be a slight acceleration of the pulse-rate and respiration, but these will subside in a minute or two in the normal, or in those with good reaction. A marked dyspnea or tachycardia, especially if it persists, would place the patient in Class IIa or IIb. A Class III patient would probably not be able to perform more than five or six swings of the dumb-bell. However, in this class the appearance and the subjective complaints are enough to fix them without exercise.

One great object of trying to classify patients is to prevent their running into Class III. A Class I and Class IIa patient will probably give no trouble, and there is a fair chance that Class IIb may not. Class III is a difficult group, and the mortality is high. The mortality would be high even if they were not pregnant.

With this definite means of sorting out patients, we have a basis upon which to base our watchfulness over them and treatment if symptoms arise. We must remember that pregnancy has an effect on the normal heart, which may be exaggerated in the abnormal one. In pregnancy the volume of blood-flow per minute is greater than it is in the same patient before pregnancy. Again, the burden that

the heart has to stand is progressive, extending over nine months, and it ends in the severe muscular strain of labor. The enlarging uterus from about the fifth month of pregnancy on displaces the heart upwards and to the left, which makes the right ventricle work under uncomfortable conditions. In the later months of pregnancy a certain amount of edema of the legs is not uncommon. Also from the pressure upward there may be a few rales in the chest, but they clear up after full inspirations. If these things can occur when the heart is normal, then it is most important to keep the patient with known cardiac abnormality under supervision. These patients should report weekly or fortnightly. A search should be made for any circulatory embarrassment, and if dyspnea, cyanosis, tachycardia, edema, pulmonary or hepatic occur, they should be put to bed, if not hospitalized. They should be treated like a non-pregnant cardiac case. Rest, sedatives, massage, restriction of fluids and salt, digitalis, cathartics and diuretics may all be needed. If the cardiac breakdown disappears, the patient may be let around again, to be put to bed again immediately if the return of symptoms demands it.

If the breakdown is repeated before the fourth month, the question of terminating the pregnancy comes up. It has both a medical and a moral aspect. With respect to the medical aspect, up until the fourth month the pregnancy can usually be terminated safely. Beyond the fourth month, in a patient with cardiac disease, it should never be attempted, and one guiding principle 'stands out clearly, and that is, that no attempt must be made to terminate pregnancy while heart-failure is present. The heart-failure must be treated first, and then, if it is better, the question of ending the pregnancy may be brought up, if it is before the fourth month. After the fourth month there is no question of terminating pregnancy in severe cardiac disease. All observers maintain it. If heart-failure occurs, it must be overcome before term, since the mortality of those who pass into labor when the heart is failing is around 50 per cent. Corwin-Herrick[18] believe that it is better to allow labor to proceed naturally. Their dictum is, that cardiac decompensation plus forceful delivery equals death. They grant that if decompensation cannot be restored through medical means, the situation is extremely grave; with forceful delivery, she is sure to die; without delivery she may die. They believe "in trusting to,

Nature more and art less." In general, if a patient cannot restore her circulation before delivery, she is not very sure of doing so after delivery. Sometimes these patients deliver themselves with surprising ease; in the 50 per cent. who succumb, it must be realized that their life expectancy was short at best, and cut down little by pregnancy with delivery.

The management of delivery is an obstetrical problem on which we are sometimes asked to give an opinion. We believe that gas should be avoided, as it already increases the undesirable cyanosis, and is contra-indicated where there is any hypertension; ether is well borne, and in itself is a cardiac stimulant. Natural delivery versus Cesarean section can be decided in individual cases. Cesarean section can be done when the cardiac condition is most favorable and there is a reasonable expectation of producing a living child. Sterilization of the patient at the same time can be done. The dangers are the ordinary complications which may occur during the first two or three days after any abdominal section. Cesarean section presupposes hospitalization and a competent operator. Natural delivery often takes place spontaneously quite satisfactorily, especially with ether anesthesia and the application of forceps in the second stage. Of course if there are obstetrical obstacles present, Cesarean section in proper hands with general or even spinal anesthesia may be advisable. We incline toward natural delivery, especially in multipara. In primipara with prolonged labor and well-restored circulation, under proper surroundings and a competent operator, the temptation to the shorter route is great.

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DISEASES OF THE BLOOD

A Review of Modern Advances

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INTRODUCTION

CLINICAL hematology embraces the so-called "blood diseases" and includes certain aspects of the reactions of the "blood system" to outside disturbances. By usage and tradition, hematology concerns itself chiefly with the formed elements of the circulating blood and with organs from which they arise. To hematology also belong certain features of hemoglobin and bile pigment metabolism and the physico-chemical mechanisms of coagulation, erythrocyte agglutination, and suspension stability. The general field of "blood chemistry" is outside the realm of hematology, although often of tremendous importance thereto.

THE PHYSIOLOGIC AND STRUCTURAL BASES OF HEMATOLOGY

The relatively modern concept of the reticulo-endothelial system[1] is still in the making and can be presented here in only the briefest outline. The cells which comprise this "system" are found in the spleen, liver, formative bone-marrow, lymphatic structures, pituitary and adrenal bodies, and more diffusely in certain connective tissues and in vascular adventitia. Reticulo-endothelial cells are of mesenchymal origin and constitute a functional unit or system in spite of their wide-spread distribution. The functions of this system in relation to hematology are conceived as follows: *first*, hematopoietic; *second*, phagocytic; and *third*, metabolic. Thus reticulo-endothelium is *the* blood-making tissue within the "blood-forming organs" (which are its chief repositories). Thus, also, in reticulo-endothelium are operative the mechanisms responsible for red-cell destruction and bile pigment elaboration and certain storage functions of protein and lipoid and cholesterol metabolism.

The blood itself, in healthy adult life, measures about 5,500 cubic centimeters in total volume of circulating fluid.[2] A little less than half of this by volume is cells and the rest is plasma. The normal ranges of red- and white-cell and platelet and hemoglobin content require no discussion here. The mechanisms of coagulation, of iso-agglutination, and of sedimentation stability are also beyond the scope of this presentation. Nor can we describe in any detail the technic of current hematologic methods. A list of these is appended to serve as a reminder for those interested in the subject.[8]

Hematologic methods (the first six are easily available for the general practitioner) are: (1) Complete blood count and differential study of (Wright's) stained films; (2) reticulocyte count (cresyl blue stain); (3) coagulation time; (4) bleeding time; (5) clot retraction; (6) tourniquet (capillary resistance) test; (7) platelet count; (8) oxydase stain; (9) supra-vital stain; (10) blood-volume determination; (11) hematocrit (cell-volume) determination; (12) van den Bergh and icterus index tests; (13) micrometer measure of cell diameters; (14) blood viscosity; (15) sedimentation stability of erythrocytes; (16) blood typing and agglutination tests; (17) erythrocyte fragility; (18) prothrombin time; (19) anti-thrombin; (20) fibrin determination; (21) other blood chemical estimations (calcium, cholesterol, *etc.*); (22) sickle-cell anemia test.

THE ANEMIAS

From the standpoint of etiology, the anemias may be classified as (1) posthemorrhagic; (2) hemolytic; and (3) those caused by interference with blood formation (including aplastic, myelophthisic, and pernicious). It must be admitted at once that many cases of anemia are of mixed or obscure etiology and cannot easily be pigeon-holed.

Acute posthemorrhagic anemias result from sudden loss of blood from the body or into the body cavities. Among the more usual types of causative hemorrhage are traumatic, postpartum, gastro-intestinal, uterine, operative and postoperative, and hemorrhage of ruptured ectopic gestation. A healthy adult can stand the loss of a pint of blood with little or no disturbance. The sudden loss of a quart of blood usually produces some symptoms from reduced blood volume and is followed by moderate anemia. The average adult

who suddenly loses one-third or more of his blood (*i.e.*, 1,800 to 2,000 cubic centimeters or more) may succumb unless emergency measures are taken to restore circulating fluid volume. Death in such cases is usually the result of reduced blood volume rather than "anemia" *per se*.

The symptoms of acute posthemorrhagic anemia are essentially those of "shock" plus those of the etiologic agent itself. For an hour or two after a severe hemorrhage a red-cell count and hemoglobin estimation show no significant change; but there is usually a well-marked leukocytosis. This leukocytosis is higher in concealed hemorrhage (peritoneal, intracranial, *etc.*) than in external hemorrhage. At this stage there is a markedly reduced blood volume. From now on, in a severe non-fatal hemorrhage, there is rapid resorption into the blood-stream of tissue fluids with consequent "dilution" of red cells and hemoglobin. The full restoration of blood volume is nearly coincident, therefore, with the greatest degree of "anemia." This point in the human is reached, as a rule, in from one to four days. Then begins the gradual process of red-cell regeneration. Reticulocytes and other young forms of erythrocytes appear usually within forty-eight to seventy-two hours after the hemorrhage. At the same time an increase in blood-platelets occurs. The new-formed red cells are poor in hemoglobin. This substance therefore lags behind in the recovery figures, thus producing the so-called hypochromatic type of anemia (*i.e.*, anemia with low "color index"). Eventual return of the blood to normal may require from one to six months.

There are several very practical points inherent in the physiology of hemorrhage. *First*, within an hour or two of a violent hemorrhage, do not expect to find any significant reduction in hemoglobin or red-cell figures. A blood count at this stage shows nothing important except neutrophilic leukocytosis. *Second*, if the blood count within an hour of the hemorrhage shows marked anemia it means that the patient was *anemic before the hemorrhage occurred*. *Third*, steadily falling red-cell and hemoglobin figures for twenty-four to thirty-six hours after a severe hemorrhage do not *necessarily* indicate continued or recurrent hemorrhage. *Fourth*, during this period a falling blood-pressure (after initial shock stage) calls for emergency treatment.

The *treatment* of acute hemorrhage may be epitomized as follows: *first*, stop the hemorrhage locally if possible; *second*, treat shock by rest, morphine, warmth, *etc.*; *third*, replace blood volume by blood transfusion if possible or by repeated intravenous saline injections if absolutely necessary. The subsequent treatment is the same as for chronic secondary anemias in general, which will be discussed later.

Chronic posthemorrhagic anemias result from repeated or continuous non-fatal hemorrhages. Important causes of this kind of hemorrhage are peptic ulcer, hemorrhoids, carcinoma of the stomach, caecum, or colon, ulcerative colitis, and uterine fibroma, polypus, *etc.* Less frequently the cause is indicated by hematuria, hemoptysis, or epistaxis.

The blood-picture in such anemias is almost always of the "low color index" (hypochromatic) type. There is often a slight leukocytosis. The platelets are normal or increased in numbers. As long as erythropoietic functions remain active there is usually evidence of such activity in the form of polychromasia, anisocytosis, poikilocytosis, some basic stippling, occasional nucleosis of erythrocytes, and reticulocytosis. If unchecked and progressive this type of anemia may terminate in the picture of profound aplastic anemia in which the above features are characteristically lacking.

Successful treatment depends upon finding the source of the "blood leak" and checking or removing its cause whenever possible. The rest of the treatment will be discussed in connection with the next group.

The symptoms of anemia in general are weakness, palpitation, functional murmurs, dyspnea, vertigo, throbbing arteries, low diastolic blood-pressure, nervousness, anorexia, dyspepsia, edema, and ofttimes fever.

Chronic secondary anemias of mixed or uncertain etiology include, in addition to the above group, anemias caused by focal infections, certain other chronic infections (*e.g.*, tuberculosis, rheumatism, syphilis, *etc.*), parasitic diseases, certain endocrine disorders (*e.g.*, myxedema), anemia of pregnancy, certain infantile anemias and those due to dietary deficiencies, anemia of nephritis, cachexia of malignancy, and anemia of leukemia and of purpura hemorrhagica, *etc.* The predominating mechanism in some of these is hemorrhage;

who suddenly loses one-third or more of his blood (*i.e.*, 1,800 to 2,000 cubic centimeters or more) may succumb unless emergency measures are taken to restore circulating fluid volume. Death in such cases is usually the result of reduced blood volume rather than "anemia" *per se*.

The symptoms of acute posthemorrhagic anemia are essentially those of "shock" plus those of the etiologic agent itself. For an hour or two after a severe hemorrhage a red-cell count and hemoglobin estimation show no significant change; but there is usually a well-marked leukocytosis. This leukocytosis is higher in concealed hemorrhage (peritoneal, intracranial, *etc.*) than in external hemorrhage. At this stage there is a markedly reduced blood volume. From now on, in a severe non-fatal hemorrhage, there is rapid resorption into the blood-stream of tissue fluids with consequent "dilution" of red cells and hemoglobin. The full restoration of blood volume is nearly coincident, therefore, with the greatest degree of "anemia." This point in the human is reached, as a rule, in from one to four days. Then begins the gradual process of red-cell regeneration. Reticulocytes and other young forms of erythrocytes appear usually within forty-eight to seventy-two hours after the hemorrhage. At the same time an increase in blood-platelets occurs. The new-formed red cells are poor in hemoglobin. This substance therefore lags behind in the recovery figures, thus producing the so-called hypochromatic type of anemia (*i.e.*, anemia with low "color index"). Eventual return of the blood to normal may require from one to six months.

There are several very practical points inherent in the physiology of hemorrhage. *First*, within an hour or two of a violent hemorrhage, do not expect to find any significant reduction in hemoglobin or red-cell figures. A blood count at this stage shows nothing important except neutrophilic leukocytosis. *Second*, if the blood count within an hour of the hemorrhage shows marked anemia it means that the patient was *anemic before the hemorrhage occurred*. *Third*, steadily falling red-cell and hemoglobin figures for twenty-four to thirty-six hours after a severe hemorrhage do not *necessarily* indicate continued or recurrent hemorrhage. *Fourth*, during this period a falling blood-pressure (after initial shock stage) calls for emergency treatment.

The *treatment* of acute hemorrhage may be epitomized as follows: *first*, stop the hemorrhage locally if possible; *second*, treat shock by rest, morphine, warmth, *etc.*; *third*, replace blood volume by blood transfusion if possible or by repeated intravenous saline injections if absolutely necessary. The subsequent treatment is the same as for chronic secondary anemias in general, which will be discussed later.

Chronic posthemorrhagic anemias result from repeated or continuous non-fatal hemorrhages. Important causes of this kind of hemorrhage are peptic ulcer, hemorrhoids, carcinoma of the stomach, caecum, or colon, ulcerative colitis, and uterine fibroma, polypus, *etc.* Less frequently the cause is indicated by hematuria, hemoptysis, or epistaxis.

The blood-picture in such anemias is almost always of the "low color index" (hypochromatic) type. There is often a slight leukocytosis. The platelets are normal or increased in numbers. As long as erythropoietic functions remain active there is usually evidence of such activity in the form of polychromasia, anisocytosis, poikilocytosis, some basic stippling, occasional nucleosis of erythrocytes, and reticulocytosis. If unchecked and progressive this type of anemia may terminate in the picture of profound aplastic anemia in which the above features are characteristically lacking.

Successful treatment depends upon finding the source of the "blood leak" and checking or removing its cause whenever possible. The rest of the treatment will be discussed in connection with the next group.

The *symptoms* of anemia in general are weakness, palpitation, functional murmurs, dyspnea, vertigo, throbbing arteries, low diastolic blood-pressure, nervousness, anorexia, dyspepsia, edema, and ofttimes fever.

Chronic secondary anemias of mixed or uncertain etiology include, in addition to the above group, anemias caused by focal infections, certain other chronic infections (*e.g.*, tuberculosis, rheumatism, syphilis, *etc.*), parasitic diseases, certain endocrine disorders (*e.g.*, myxedema), anemia of pregnancy, certain infantile anemias and those due to dietary deficiencies, anemia of nephritis, cachexia of malignancy, and anemia of leukemia and of purpura hemorrhagica, *etc.* The predominating mechanism in some of these is hemorrhage;

in others, hemolysis; in others, interference with normal erythro-poieses; and in many, a combination of these mechanisms.

The treatment of chronic secondary anemia has advanced con-siderably in the past few years, the initial impetus coming from Whipple's[4] work and from the brilliant success of Minot[5] and his associates in pernicious anemia. Despite this progress, however, it is still as true as ever that the successful management of chronic secondary anemia depends first and foremost on painstaking study to determine the cause, and on careful eradication, by specific me-dicinal, dietary, roentgenologic, or surgical means of any remedial cause found. Additional methods of treatment are as follows:

Diet.—The liver and kidney of mammals and birds contain something which accelerates hemoglobin and red-cell regeneration in posthemmorrhagic anemia of dogs (Whipple). The use of these sub-stances in human secondary anemias (posthemorrhagic or otherwise) is sometimes distinctly beneficial though rarely comparable in dramatic efficiency to their use in pernicious anemia. It is to be hoped that Whipple will succeed still further[6] in isolating the frac-tion of liver which is chiefly responsible for this general stimulating effect. It is obviously a somewhat different fraction than that isolated by Cohn and Minot for pernicious anemia. In any event, it is the consensus of opinion that liver (preferably calf's liver rare or raw) is more effective in secondary anemia than the now available liver extracts. In addition, Whipple has found that apricots, peaches, prunes and apples head the list of fruits in red-blood building properties. Finally, a high vitamin content is advised, including the vitamins of fresh fruit, of cod-liver oil, of wheat germ oil, and of leafy greens. A sort of "shotgun" dietary prescription for anemia therefore includes a daily intake of 200 to 500 grams of calf's liver (or kidney) and plenty of apricots, peaches, orange or tomato juice, leafy greens and salads, and cod-liver oil.

Ultraviolet ray is perhaps of some value as a supplement to vitamin feeding. It should be given in small, carefully regulated dosage (either by lamp or sunlight).

Iron medication is being enthusiastically revived, with emphasis on large dosage rather than on any "pet" brand or type of iron compound. It is best given by mouth.

Arsenic is employed less than ever in the treatment of anemia. Its value is questionable.

Copper is recommended[7] in minute dosage (four to five milligrams daily of copper sulphate) in the treatment of obscure secondary anemia, together with iron and diet.

Blood transfusion is one of the very best methods of "pulling up out of the rut" a sluggish resistant case of chronic secondary anemia of almost any type.

The hemolytic anemias may be *secondary* to various infections (*e.g.*, streptococcemia) and infestations (*e.g.*, malaria), to certain chemical poisons (*e.g.*, lead, phenylhydrazin) or to metabolic toxins (*e.g.*, "hemolytic anemia of pregnancy") or they may be *primary* (*i.e.*, of unknown etiology). Of the primary hemolytic anemias, the most important are hemolytic ictero-anemia (hemolytic jaundice), sickle-cell anemia, splenic anemia and Banti's disease. Pernicious anemia, although exhibiting definite hemolytic features, belongs in the group due to abnormalities of red-cell formation (Minot).

The characteristic features present, to a greater or less extent, in all cases of hemolytic anemia are: slight icterus of non-obstructive type, urobilinuria (but otherwise acholuric) and increase in indirect van den Bergh reaction of the plasma. Many of them exhibit a rather constant reticulocytosis and some exhibit splenomegaly. Hemoglobinuria is a rare manifestation and occurs only in severe acute hemolysis (as after transfusion of incompatible blood, in "blackwater fever," after extensive burns, *etc.*), and in that rare disease known as paroxysmal hemoglobinuria which is probably of luetic etiology.

Hemolytic jaundice (hemolytic ictero-anemia) is usually hereditary but may be "acquired." Its etiology is unknown. The symptoms of the familial forms are, during youth, merely those of slight non-obstructive jaundice and slight anemia. Later periods of acute increase in anemia and jaundice with bouts of fever, abdominal pains and vomiting occur. Physical examination reveals marked splenomegaly, slight jaundice and pallor and slight enlargement of the liver. About half the cases in adult life have gall-stones, which may complicate the picture. The laboratory diagnosis rests on demonstration of the characteristic *increase in fragility* of the erythrocytes

when tested in gradations of hypotonic salt solution. Normal red-blood cells and, indeed, those of practically all other conditions (including the various anemias and obstructive jaundice) begin to hemolize at .450 per cent. salt solution or less and are completely hemolized at .325 per cent. or less. In hemolytic jaundice the erythrocytes hemolize at a point much nearer the tonicity of "normal salt" solution, so that in this disease hemolysis begins at .650 per cent. to .500 per cent. and is complete at .450 per cent. to .400 per cent. Additional laboratory findings are high indirect van den Bergh, moderate to marked hypochromatic anemia with normal or elevated leukocytes and platelets. The red cells are often smaller than normal and from 10 to 40 per cent. reticulated erythrocytes are usually found. The *treatment* in severe cases is *splenectomy*. A clinical cure or "near cure" is obtained by this operation in over 90 per cent. of cases of familial hemolytic jaundice. The *acquired* form of the disease begins later in life and is more severe. The results of splenectomy, although sometimes justifying the risk involved, are not very satisfactory.

Sickle-cell anemia is also hereditary and largely confined to negroes or persons with some negro ancestry. The symptoms are not unlike those of hemolytic ictero-anemia, although crises of abdominal pain and rheumatic-like attacks are more frequent in sickle-cell anemia. Also, in the latter disease the spleen is rarely very large and undergoes marked atrophy in the older (adult) cases. The fragility test is near normal. The indirect van den Bergh is increased. The leukocytes are normal or elevated, as are the platelets. The anemia is of secondary (hypchromatic) type. Reticulocytosis is often marked (5 to 20 per cent.). The diagnosis depends upon demonstration of the characteristic "sickling" which appears in a drop of blood sealed in vaselin after a few hours. (See Fig. 1.) The treatment is merely that of anemia. Splenectomy[8] has failed to benefit permanently two cases known to the author, although there are a few favorable reports.

Anemia of pregnancy[9] is very common in its milder form (*i.e.*, 3,500,000 to 4,000,000 red cells with 65 to 75 per cent. hemoglobin), and often goes unrecognized and requires no treatment. A few cases of severe hemolytic anemia resembling pernicious anemia are recorded which require transfusion, liver therapy, and occasion-

FIG. 1.

Sickle-cell formation.

FIG. 2.
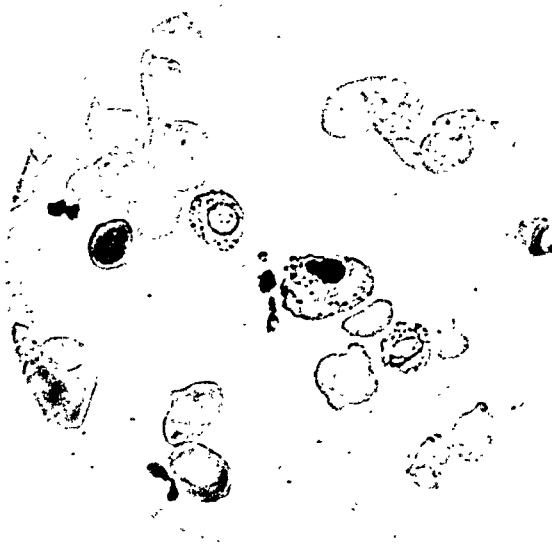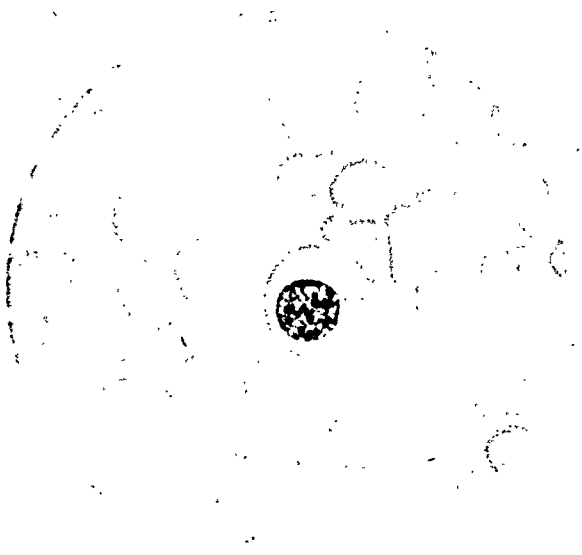
FIG. 3.

FIG. 2. The blood in pernicious anemia showing a classical megaloblast. Note also paucity of platelets and leukocytes (none shown) and megalocytosis.

FIG. 3. Red cell changes in Von Jaksch's anemia. Note Cabbott rings, basin stippling and nuclear remnant in red cell.

ally therapeutic abortion. In my experience the presence of slight leukocytosis, normal or increased platelets, and usually the hypochromatic character of the anemia and the presence of free hydrochloric acid in the gastric juice all together combine to separate these anemias of pregnancy quite sharply from pernicious anemia.

Splenic anemia and Banti's disease are designations for the early and late stages respectively of the same pathologic process. The etiology is unknown. The symptoms often begin in adolescence. They are weakness, digestive upsets and epistaxis. At this time examination reveals moderate anemia and splenomegaly. Later gastric hemorrhages are common. This first stage lasts usually from three to five years. Then jaundice and increasing hepatic enlargement appear and in a few months ascites with atrophic cirrhosis of liver, cachexia and increasing tendency to gastric and esophageal hemorrhages (from varices) mark the full-blown picture which usually terminates in death within a year. At this stage the anemia is often severe. It is hypochromatic in type. Leukocytes are reduced (2,000 to 4,000 per cubic millimeter). Reticulocytosis is usually absent. "Fragility" is normal, or there may even be an increase in resistance of red cells to hemolysis. Platelets are usually diminished. The *treatment* is splenectomy, and the earlier the operation, the better the outlook, but at best this is none too good.

The Aplastic Anemias: Myelophthisic Anemias: Pernicious Anemia: Chlorosis.—Idiopathic (*primary*) *aplastic anemia* is a rare disease. It occurs chiefly in young adults. The symptoms are those of rapidly increasing anemia with (symptomatic) purpura hemorrhagica. Death occurs within a few weeks to a few months as a rule. Physical examination reveals pallor, fever, "functional" cardiac murmurs, petechiae, and mucous membrane hemorrhages. The blood shows profound aplastic anemia (*i.e.*, practically no poikilocytosis, no anisocytosis, no polychromasia, no stippling, no nucleosis, no reticulocytosis) together with neutrophilic leukopenia and thrombocytopemia. The color index is about one. At autopsy the bone-marrow is found generally "aplastic." Transfusions may prolong life for a time. Fetal calf's liver and raw fresh bone-marrow have recently been recommended. Treatment is essentially hopeless. (Figs. 2 and 3.)

Secondary aplastic anemia may result from any form of long-

standing chronic anemia and, in addition, may be caused by poisons such as benzol and trinitrotoluol and by radium and X-ray. The treatment and the prognosis in these cases depend on the stage of the disease and the removability of the cause. Transfusions are sometimes lifesaving (as in early stages of benzol poisoning).

Pernicious anemia was yesterday a leper among diseases, begging alms at the gates of our temple. Today the miracle touch of the healer has transformed this creature of despair. We practitioners of medicine, armed with new power, are duty-bound to be ever alert that we may miss no opportunity to participate personally in this modern-day miracle.

An adequate discussion of pernicious anemia is here impossible. The important practical clinical and laboratory data are tabulated below, with a few selected references designed to guide the interested student through the main channels of recent progress.

Definition.—A chronic disease, usually exhibiting one or more remissions, affecting both sexes, rarely manifest before thirty-five, sometimes familial, with a "normally" fatal course averaging about three years, characterized by severe hyperchromatic (megalocytic) anemia with hemolytic features (in relapses), by permanent achlorhydria, frequently by degenerative changes in the central nervous system, and finally characterized by an almost specific response (blood remission) to treatment by liver, liver extract, desiccated hog's stomach, and by meat predigested in a normal human stomach.

Important Symptoms.—(1) General body structure and circulatory system: weakness, dyspnea, palpitation, precordial pains, vertigo, headache, and usually moderate loss of weight and feverishness in relapse.

(2) Blood system: as above, plus pallor and slight hemorrhagic manifestations (epistaxis, melena, hematemesis, metrorrhagia, petechiae, *etc.*).

(3) Central nervous system: mental depression, sometimes psychosis, delirium and coma; numbness, paresthesias and ataxia of extremities, sometimes girdle sensations and sphincteric disturbances (rare).

(4) Gastro-intestinal system: sore tongue, anorexia, nausea, gaseous dyspepsia, constipation or diarrhea and abdominal pains.

Important Signs.—(1) General and circulatory: low blood-pres-

sure, high pulse-pressure, functional murmurs, slight cardiac dilatation, edema, engorgement of liver, weakness without emaciation, and fever in relapse.

(2) Blood system: lemon-yellow or pale copper color of skin, occasionally petechiae and retinal hemorrhages, sometimes moderate enlargement of spleen and liver.

(3) Central nervous system: diminution or loss of sense of vibration and of position of lower extremities, disturbances of tendon reflexes, and sometimes positive Babinski reflex.

(4) Gastro-intestinal system: glossitis or atrophic lingual mucosa.

Important Laboratory Findings.—(1) Blood: anemia with high color index (*e.g.*, red cells, 1,500,000; hemoglobin, 40 per cent.; color index = 40/30 = 1.3); leukopenia (2 to 5,000 white cells per cubic millimeter); thrombocytopenia (10 to 100,000 platelets per cubic millimeter); megalocytosis; occasionally megaloblasts and normoblasts; bilirubinemia (*i.e.*, increased indirect van den Bergh); reticulocytosis in response to liver therapy or at onset of remission; specific increase in blood uric acid and blood cholesterol at onset of liver-induced remission.

(2) Urine: urobilinuria in relapse. Quantitive increase in urine at onset of remission.

(3) Gastric analysis: constant and persistent achlorhydria, even by histamin method.

Differential Diagnosis.—Pernicious anemia is to be differentiated from various chronic secondary anemias in which the color index is usually less than one and in which the leukopenia, thrombocytopenia, and achlorhydria characteristic of pernicious anemia are usually lacking. There are a few anemias, however, in which the differential diagnosis may be difficult. The anemia of Dibothryocephalus latus infestation[10] is rarely like that of pernicious anemia. When present in this form, however, it too responds to liver therapy. Sprue anemia is said to simulate pernicious anemia in some cases, though usually gastric analysis reveals free hydrochloric acid and there is marked emaciation in sprue. Here, too, a specific recovery occurs under liver therapy.[11] Gastric carcinoma and polyposis are rarely associated with a picture similar to pernicious anemia. Many of the older cases so reported do not fit

modern conceptions of the meaning of the syndrome. In a few instances it would seem that the two diseases co-exist.

Treatment and the Effects of Treatment.—The work of Minot and Murphy[5] first, and subsequently that of Cohn[12] and of Castle,[13] and of Sturgis and Isaacs[14] and Sharp[14] constitutes an astonishing, brilliant chapter in medical progress. In brief, the treatment of pernicious anemia consists in the per oral administration of an adequate amount of raw or cooked liver of beef, pig, calf, or chicken. From 200 to 800 grams daily may be required at the start. Later the maintenance dose may be reduced to about 100 grams daily, sometimes less, sometimes more. Potent liver extracts may also be used, but in relatively larger doses, or desiccated hog's stomach may be employed with equally good results. The response to effective therapy varies somewhat with the severity of the anemia and the amount of liver. The first sign of improvement comes within a few days when the reticulocytes begin to rise. At the same time subjective improvement may be noted. After a week to ten days the reticulocyte increase reaches its peak (from 10 to 50 per cent. of the red cells being reticulated). The magnitude of the reticulocyte response varies directly with the severity of the anemia.[15] Massive doses of the effective material induce the reticulocyte crisis sooner than smaller doses. Following the reticulocyte crisis (which promptly disappears) there is a steady rise in red cells and hemoglobin and dramatic improvement in the patient. The blood usually reaches normal figures within two to three months. Treatment must then be continued indefinitely. If treatment is stopped or inadequate, most patients begin to relapse within a few weeks to a few months. This is therefore clearly a "replacement" therapy and not a cure. Taking it by and large, however, there is nothing more delightfully satisfactory in the practice of medicine than the recovery of these patients under proper therapy. Appetite and strength return, depression vanishes, edema and circulatory embarrassment disappear, digestion and bowel function become normal, and glossitis and paresthesias often subside. Cases with advanced postero-lateral sclerosis of the cord are not cured in this respect, but some are astonishingly benefited. Achlorhydria persists but apparently produces no symptoms.

Additional forms of treatment are rarely necessary, except an

initial blood transfusion in a moribund patient. Dilute hydrochloric acid is advised by some, but is certainly not necessary to secure a remission. A very few cases of pernicious anemia have shown progressive central nervous system damage in spite of blood recovery under treatment.

In general, it may be said that a severe anemia which fails to respond to this therapy *adequately supplied* is not pernicious anemia.

The myelophthisic anemias are caused by abnormal "growths" in the bone-marrow, as in metastatic carcinoma, the leukemias, multiple myeloma, *etc.* The blood-picture may terminate as an aplastic one but usually there are to be found at all stages some evidences of bone-marrow "irritation" and "regeneration" (*e.g.,* normoblasts, myelocytes, plentiful platelets and often leukocytosis).

Chlorosis has apparently vanished. One sees many cases of obscure or perhaps "idiopathic" secondary (or "chlorotic") types of anemia in all ages and in both sexes. None of these, however, fits the classical picture of chlorosis with its much-emphasized therapeutic test of curability by iron medication.

The erythroblastic anemias of infancy[16] (including von Jaksch's anemia) constitute an important chapter in clinical hematology. The characteristic features are profound anemia with color index of near unity, marked red-cell nucleosis (usually normoblasts) sometimes constituting 50 per cent. or more of the total nucleated cells of the blood, reticulocytosis, moderate to marked leukocytosis usually showing an increase in young forms (myelocytes, band forms, *etc.,*) and often a moderate eosinophilia. The treatment is blood transfusion, proper diet and plentiful supply of vitamins. If taken early, many can be cured. When the full-blown picture of von Jaksch's anemia, with splenomegaly, *etc.,* has developed, the prognosis is poor (in spite of statements in the older literature to the contrary).

POLYCYTHEMIA

Relative polycythemia occurs in dehydration, as from vomiting, diarrhea, water starvation, severe burns, and pulmonary edema from gas poisoning.

Absolute polycythemia connotes not only increased concentration of red cells in the blood but more especially an increase in the total number of red cells in the body; hence, also, an increased blood

volume. This may be *secondary*, as in chronic heart and pulmonary disease (including Ayerza's disease) and in the chronic anoxemia incident to living in high altitudes. The most striking absolute polycythemia is the *primary* form known as:

Polycythemia vera (erythremia, Osler-Vaquez's disease) is characterized clinically by chronic cyanosis, splenomegaly, circulatory disturbances, headache, vertigo, thromboses, hemorrhages, and often premature arteriosclerosis. The disease ends fatally in six to eight years as a rule. Blood count shows marked increase in red cells (7 to 14 million) and hemoglobin (120 to 180 per cent.) together with moderate leukocytosis (8 to 20,000) and increase in platelets. Sometimes there is a leukemoid appearance of the blood (myelocytes, *etc.*). Blood volume is markedly increased, as is also the cell volume. The plasma volume is usually normal. Basal metabolism is increased, and so is blood viscosity.

Treatment is largely palliative. Venesection gives temporary relief. X-ray treatment of the long bones has produced improvement in some cases. Ominous leukopenia, however, usually comes before significant reduction in red cells in the writer's experience. *Phenylhydrazin hydrochlorid* has given the most satisfactory results. The drug is dangerous and its proper use must be thoroughly understood before instituting treatment.[17] A fairly safe initial course is: capsules phenylhydrazin hydrochloride (each 0.1 gram), No. xx. Sig. one capsule after each meal t.i.d. for five days, then reduce to one capsule daily for five days.

THE LEUKEMIAS

The acute leukemias (myelogenous and lymphatic) are affections of children and of young adults, although chronic leukemias of older people frequently terminate in an "acute stage." There are no noteworthy differential features between acute myelogenous and acute lymphatic leukemia except in expert study of the blood. With oxydase staining, the granulation of the young myelocytes may sometimes be found, thus marking the case as myelogenous. However, it is occasionally impossible to separate acute lymphoblastic and acute myeloblastic leukemias by any known clinical means.

The blood-picture in the acute leukemias is as follows: leukocytes from 50 to 500,000 per cubic millimeter with 80 to 100 per cent. of

the cells being either myeloblasts or lymphoblasts. Anemia is of the secondary type and rapidly progressive. Platelets are often reduced.

The symptoms are those of severe sepsis associated with stomatitis, ulcerative angina, moderate cervical and mediastinal adenopathy, little or no superficial adenopathy, slight splenomegaly, hemorrhages, fever and progressive anemia. Death terminates the picture in a few weeks to a few months, as a rule, although *sometimes* a partial remission occurs and the case passes over into a subacute or chronic type of leukemia.

Treatment of the acute leukemias is essentially hopeless. Transfusions help for a time. Oral antiseptics, liver diet, and cod-liver oil in large dosage are recommended. X-ray therapy is apparently of no value except in the chronic forms of the disease.

The chronic leukemias are similarly of *myelogenous* and *lymphatic* types and both of these occur also in the so-called *aleukemic* form.

Chronic myelogenous leukemia is a disease of adults. The onset is insidious as a rule but may be ushered in with dramatic suddenness (*e.g.*, intractable bleeding from tooth extraction, or apoplexy). The commonest onset symptoms are local discomfort due to the enlarged spleen, weakness, pallor, and vertigo or tinnitus aurium. Petechiae and other hemorrhagic and thrombotic manifestations occur. Gastro-intestinal disturbances, jaundice, pruritus, fever and sweats are common later in the disease. Priapism (always mentioned in the literature) is *extremely rare.*

Examination reveals tremendous splenic and considerable hepatic enlargement with little or no general lymph-node enlargement. Petechiae, retinal hemorrhages, and slight jaundice and fever are common. Anemia is progressive but rarely profound until near the end. The characteristic laboratory findings are: leukocytosis, 100,-000 to 1,000,000 per cubic millimeter, with differential showing increase in all elements but most especially in the polymorphonuclear neutrophiles, myelocytes and eosinophiles. Blood-platelets are increased. Blood uric acid figures are usually high. Basal metabolism is elevated. The average duration of life is about four years from onset of symptoms.

Chronic lymphatic leukuemia is also a disease of adults.

course is more prolonged and its symptoms milder than those of chronic myelogenous leukemia. The symptoms are in general similar except that glandular enlargements are more prominent (cervical, axillary, inguinal, epitrochlear, mediastinal, abdominal) and splenomegaly less marked. The blood count shows 80,000 to 500,-000 white-blood cells per cubic millimeter of which 90 per cent. or more are lymphocytes. Anemia and thrombocytopenia are progressive. The average duration of life is five to eight years.

Treatment of chronic leukemia (both forms) is best accomplished by X-ray of spleen and long bones. Remission of the disease can be thus usually induced for a time. Of the drugs, benzol is the best but is dangerous and must be used wisely. It is administered in capsules, each of which contains 0.5 grams of benzol and 0.5 grams of olive oil. Two such capsules are given four times daily until the leukocyte count drops to about 20,000, or until a significant reduction in blood-platelets occurs.

Aleukemic leukemia is a term which should be applied only to those rare cases[18] in which the internal organs at autopsy (or biopsy) show typical leukemic changes (either lymphatic or myelogenous) while the blood shows *no* leukemic changes at all. The more common conditions (phases of leukemia in remissions and as a result of treatment) in which the total leukocyte count may be normal but in which the differential count shows definite leukemic character, are more properly designated as "leukopenic" or "subleukemic" leukemia rather than "aleukemic leukemia."

Leukemoid Blood Reactions in Various Conditions Other than Leukemia.—*Intense infections* of septic type may occasionally produce a blood-picture simulating either form of leukemia. Pneumonia may be encountered with 80,000 leukocytes of which 20 to 40 per cent. may be myelocytes. Whooping cough sometimes presents a similar leukocytosis with 80 per cent. of the cells being lymphocytes.

Infectious mononucleosis (glandular fever) may not only simulate the blood-picture of acute leukemia, but, on account of its angina, fever, cervical adenopathy, and moderate splenomegaly, presents similar clinical features as well. In "mononucleosis," however, hemorrhagic symptoms and anemia are lacking and the blood-picture is not completely similar to leukemia in that the total leukocyte count rarely exceeds 30,000 per cubic millimeter and the

differential shows rarely more than 70 per cent. lymphocytes in contrast to the usual 95 to 98 per cent. lymphoblastosis or myeloblastosis of acute leukemia. Patients with infectious mononucleosis recover in a few weeks, although relative lymphocytosis and slight cervical adenopathy may persist for months.

Agranulocytic angina (Schultz) may simulate acute sub-leukemic (leukopenic) lymphatic leukemia. This disease is characterized by rapidly developing stomatitis and angina (with sometimes necrotic patches in the mucosa of rectum or vagina), with septic fever and a most striking leukopenia. The blood count shows from 100 to 1,500 leukocytes per cubic millimeter, of which 90 to 100 per cent. are lymphocytes. Oxydase stain shows practically no granular leukocytes (*i.e.*, no polymorphonuclears, no myelocytes, no eosinophiles, no monocytes). The platelets and erythrocytes are not significantly affected. (This differentiates these cases from aplastic anemia, although instances of the latter are now unfortunately being reported under the designation of agranulocytic angina.) Over 90 per cent. of the cases thus far reported have died. A few have had remissions and diet in a subsequent relapse. The treatment[19] is: (1) frequent blood transfusions, with venesection if plethora develops; (2) "stimulative" X-ray therapy over long bones and sternum; (3) local antiseptic measures in mouth and throat; (4) elimination of allergenic factors (Pepper); (5) liver diet, *etc.*

The leukemoid blood reactions which occur in some cases of carcinoma (especially with bone-marrow metastasis) sarcoma, Hodgkin's disease[20] and leukosarcoma are rarely of such magnitude as to cause much confusion in diagnosis. *Chloroma* is merely a special manifestation of leukemia, and needs no further discussion here. The disease known as "*multiple myeloma*" produces a myelophthisic anemia but no true leukemic blood-picture.

Before leaving the subject of the leukemoid blood reactions the student of hematology must familiarize himself with the rejuvenated "Arneth Index," as modified by Schilling[21] and others. The differential study of the neutrophilic leukocytes in disease yields valuable information. But even the simplified "Schilling Hemogram" involves a certain mathematical laboriousness together with some technical uncertainties and some unproven assumptions that, according to this reviewer, altogether impair its usefulness as a routine

procedure. The prognostic implications of the "shift to the left" are hardly more trustworthy than the simpler "index" obtained by the more ordinary data of total leukocyte count and total neutrophil percentage together with the "impressions" one gains inevitably from inspection of a stained film (*i.e.*, presence of myelocytes, *etc.*).

HEMORRHAGIC DISEASES

Purpura hemorrhagica (thrombocytopenic) occurs as a *primary* or essential disease (Werlhof's disease) and as a *secondary* syndrome in a variety of conditions which cause diminution of blood-platelets. The syndrome of thrombocytopenia, be it of "idiopathic" or of "secondary" origin, is characterized in fully developed form by *clinical manifestations* of hemorrhage (purpura, ecchymoses, easy bruising, bleeding from mucous membranes and abnormal post-traumatic bleeding) and by the following "*laboratory*" *findings*: (1) thrombocytopenia (*i.e.*, platelets less than 100,000 per cubic millimeter); (2) prolonged bleeding time (Duke); (3) normal coagulation time; (4) absent clot retraction; and (5) positive capillary resistance (tourniquet) test. (Fig. 4.)

Essential thrombocytopenic purpura (Werhlhof's hemorrhagic purpura) is a disease of unknown etiology and of vagrant and unpredictable course. It is more common in childhood but no age is exempt. Both sexes are affected and the disease is sometimes (rarely) hereditary. It occurs in acute, chronic, and intermittent forms. The onset symptoms (petechiae and hemorrhages) are often abrupt. Hemorrhages may be in the form of epistaxis, bleeding gums, menorrhagia, metrorrhagia, melena, hematemesis, hematuria, cerebral and subarachnoid extravasations, hematomyelia and hematoma. In contrast to hemophilia one almost never sees hemarthrosis in this disease. Physical examination reveals petechiae, slight fever in active attacks, and often a palpable spleen. The laboratory findings are those listed above, under the syndrone of thrombocytopenia, plus the picture of posthemorrhagic anemia (q.v.). The treatment[22] is: (1) blood transfusion; (2) intramuscular protein (whole blood, sterilized, milk, *etc.*) injections; (3) liver diet, *etc.*; (4) X-ray irradiation of the spleen; and (5) splenectomy. In well-established chronic cases splenectomy is the only effective treatment and results in "near" cure or symptomatic relief of most cases. Focal

Fic. 4.
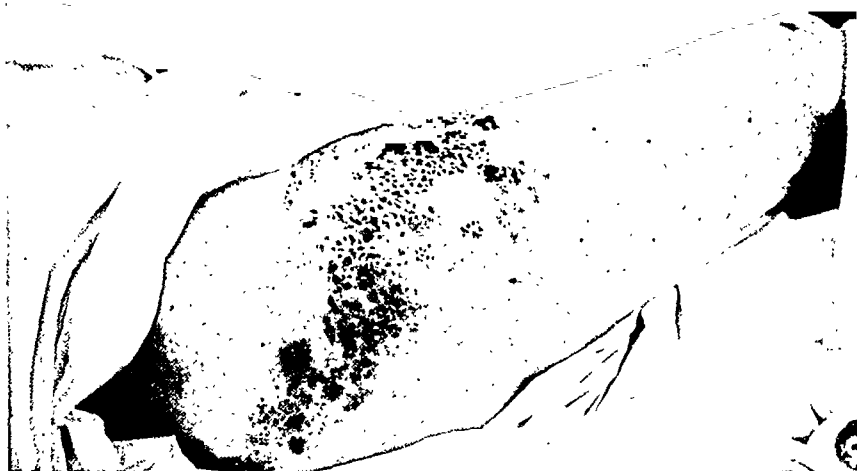
Thigh of patient with purpura hemorrhagica who developed an intercurrent herpes zoster.

infections (tonsil sepsis, *etc.*) should theoretically be removed, but great caution is urged in this connection (hemorrhage!).

Secondary thrombocytopenic purpura occurs:

(1) In certain infections (*e.g.*, overwhelming sepsis, hemorrhagic smallpox, *etc.*).

(2) In benzol poisoning (see aplastic anemia) and sometimes as a result of arsphenamin therapy.

(3) In aplastic anemia of all kinds.

(4) In pernicious anemia in relapse.

(5) In acute leukemias and some cases of chronic lymphatic leukemia.

The manifestations and findings are as described above in the "essential form." The treatment is that of the underlying condition. Repeated blood transfusion is the most important therapy. In the writer's opinion "citrate" transfusion is just as effective as "unmodified" blood.

Hemophilia is exhibited solely by males. It is transmitted *directly* by female "conductors" only, but through such intermediaries, may also be transmitted by males as well.[23] This "most hereditary of diseases" is occasionally seen, however, as a sporadic, apparently non-hereditary (but probably atavistic) manifestation. The disease is characterized by abnormal tendency to bleed from relatively slight traumatism. The hemorrhagic diathesis begins usually a few weeks to a few months after birth. If the boy sufferer survives infancy and early adolescence, there is often a characteristic deformity of the knee-joints from repeated hemarthrosis. In contrast to patients with purpura hemorrhagica, hemophiliacs rarely bleed spontaneously from mucous membranes, and do not exhibit spontaneous petechiae or splenomegaly. The essential feature of hemophilia is *prolongation of coagulation time*. Again, in contrast to purpura hemorrhagica, the bleeding time, platelet-count, and clot retraction are all normal in hemophilia.

The treatment is (1) care to avoid traumatism and (2) transfusion: to check bleeding, to correct the effects of bleeding, and to prepare the patient for some necessary operation. The effects of transfusion in correcting the clotting defect last only several days and transfusion may then have to be repeated.

Hereditary hemorrhagic telangiectasia[24] has frequently been mis-

taken for either purpura hemorrhagica or hemophilia but is easily differentiated. The lesions, while superficially resembling petechiae, are readily identified as telangiectases by pressure with a glass slide. Telangiectases fade out under pressure while petechiae do not. Furthermore, petechiae come and go within a few days, while telangiectases are more permanent. The disease is exhibited by both sexes and transmitted by both sexes. Blood studies are all normal (except for posthemorrhagic anemia) and hemorrhages are due to rupture of telangiectases and not to any known hemorrhagic diathesis.

Hereditary hemorrhagic thrombasthenia[25] and *hemorrhagic disease of the new-born* and certain other atypical hemorrhagic disorders recently described cannot be discussed in this presentation. The same remarks apply to Gaucher's disease and Niemann-Pick's disease, which sometimes exhibit slight hemorrhagic phenomena.

The hemorrhagic diathesis of obstructive jaundice is of obscure etiology. It depends apparently on hepatic degeneration and is associated with moderate prolongation of coagulation time and diminution in blood fibrinogen and, according to some observers, with diminution of available calcium. The treatment[26] is best accomplished by frequent intravenous glucose injections (5 to 10 per cent. in quantities of 500 to 1,000 cubic centimeters daily) and by blood transfusion. Calcium therapy is advised by many but has not proven itself of any value in the writer's experience.

MISCELLANEA HEMATOLOGICA

1. *The leukocyte count in general practice.*—Epidemic infections characterized by low or normal count: measles, mumps, chicken pox, influenza, malaria, typhoid fever. Epidemic infections characterized by leukocytosis: pneumonia, scarlet fever, streptococcic tonsillitis, meningitis, smallpox, trichiniasis.

2. *The differential count in general practice.*—Important causes of relative or absolute lymphocytosis: whooping cough, infectious mononucleosis (glandular fever), sometimes influenza, tuberculosis and syphilis, lymphatic leukemia, and postinfectious convalescent states (also blood of infants).

Important causes of eosinophilia.—Allergic conditions (asthma, serum sickness, *etc.*), parasitic diseases (trichiniasis, uncinariasis, *etc.*), dermatoses (eczema, *etc.*), scarlet fever, postinfectious con-

valescent states, myelogenous leukemia, some cases of Hodgkin's disease, during reabsorption of internal hemorrhage, post-splenectomy, and after-use of raw liver diet.

3. In the presence of an *"acute infection"* a leukocytosis of 20,000 or more with well-marked eosinophilia (10 to 50 per cent.) is *almost* pathognomonic of either scarlet fever or trichinasis.

4. *High reticulocyte counts* (10 to 40 per cent.) are usually found in hemolytic jaundice, sickle-cell anemia, lead-poisoning, erythroblastic anemia of infancy, pernicious anemia at end of first week of therapeutically induced remission (also sprue and Dibothryocephalus latus anemia in similar remission), new-born infants in first twenty-four hours of life, some cases of purpura hemorrhagica, some cases of acute posthemorrhagic anemia in healthy subjects, post-splenectomy in various anemias, at times in any actively "remitting" anemia (especially those of hemolytic type), and at the onset of polycythemia due to living in high altitude.

5. *Splenomegaly* occurs in diseases of hematologic interest as follows: The luekemias, hemolytic jaundice, splenic anemia and Banti's disease, Hodgkin's disease, malaria, infective endocarditis, typhoid, syphilis, tuberculosis, von Jaksch's anemia, pernicious anemia, polycythemia vera, Gaucher's disease, Niemann's disease, hepatic cirrhosis (slight), advanced cases of hereditary hemorrhagic telangiectasis (Fitz-Hugh: to be reported), sickle-cell anemia (*youthful* cases), essential thrombocytopenic purpura, amyloid diseases, rickets, and occasionally in measles and in exophthalmic goiter.

6. *Splenectomy*[27] is of real value in selected cases of hemolytic jaundice, splenic anemia, Banti's disease, and essential thrombocytopenic purpura. The operation has proved helpful in some cases of Gaucher's disease, some of luetic, tuberculous and malarial splenomegaly, and, prior to 1926, in some cases of pernicious anemia.

7. Pernicious anemia masquerades, at times, under various guises, including "valvular heart disease," "myocarditis," "angina pectoris," "Bright's disease," "psychoneurosis," "gastritis," "colitis," "malignancy," "locomotor-ataxia," "spinal-cord tumor," and "general debility." This list sounds like an advertisement for a patent medicine. Yet it is often with one or another of these diagnoses that pernicious anemia sufferers are referred.

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RECENT ADVANCES IN DRUG THERAPY

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I HAVE had some misgivings about the title of these lectures, "Recent Advances in Drug Therapy," not because I thought that I was going to speak about anything but recent advances in drug therapy, but because I was afraid that to many individuals that title might signify simply a discussion of recent discoveries of new drugs. The history of drug therapy is characterized by two types of movements, the pendular movement and the forward movement. Year after year hundreds of new preparations are introduced, exploited enthusiastically, recommended by physicians, then discredited and forgotten. The physician's greater eagerness for new preparations than for a better knowledge of how to use well-established drugs is a great factor in therapeutic pseudo-progress or the pendular movement in the history of drug therapy.

Our knowledge of drug therapy has moved forward rather rapidly in the past fifteen or twenty years by the force of new facts that have come from three general directions—and I state them in what I believe is the order of their importance at the present time—first, from the study of general principles that govern drug action and usage; second, from the better understanding of the properties and actions of established drugs and the behavior of the organism under their influence, with the view of discarding those that prove to be superfluous or of no value and improving our use of those that are retained; and third, from the study of new drugs that may prove to be of value in the treatment of disease.

It would be utterly impossible in the time at our disposal to discuss in any great detail the progress that has been made in these three phases of knowledge in drug therapy. Several subjects will be

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considered in a somewhat fragmentary way, all with the view of indicating how the average physician under the average conditions of medical practice can deal with the problems of rational drug therapy. In discussing advances in new drugs and procedures, the large numbers of minor additions to therapeutics, as well as many studies of great scientific and technical merit will have to be omitted; the present status of only some of the larger problems that possess general interest will be reviewed briefly.

It is hardly necessary to state that the fundamental distinction between empirical and rational drug therapy is, that the latter is governed by a knowledge of the mode of action of a drug and its behavior in the body. There are exceptional instances in which some of the most important remedies were used with considerable success before their mode of action was known. For example, Withering used digitalis with great success and arrived at very sound and practical principles of dosage in the treatment of dropsy without even knowing that the beneficial effects were due to an action upon the circulation. It nevertheless requires no argument that the vast accumulation of experimental and clinical pharmacology dealing with that drug, has placed digitalis therapy upon a plane incomparably superior to that of the days before such knowledge was available. In the hands of those familiar with this work the drug has indeed acquired new powers with simultaneous reduction in its dangers.

Many of the recent textbooks on therapeutics stress the importance of a thorough knowledge of the pharmacology of the commonly used drugs but, judging from the fallacious notions that are still encountered in the clinical literature, it is apparent that the importance of a knowledge of the fundamentals of the pharmacology of therapeutic agents cannot be overstressed. For example, a well-known obstetrician recently made the statement that it is dangerous to deliver the baby shortly after the administration of morphine to the mother because the morphine continued to circulate in the blood of the mother and fetus. He would not have offered that explanation for the well-known fact that it is dangerous to give morphine to the mother shortly before delivery, had he been familiar with the fact that most of the alkaloids disappear very rapidly from the blood-stream, or that at least, their concentration in the blood falls so quickly that within a few minutes their presence can rarely be

detected, the drug having been taken up by the various organs and tissues of the body. For many years it has been held that the average patient excretes about two grains of digitalis daily and utterly irrational practices have grown up around this idea which ignored a fundamental pharmacologic principle, namely, that the animal organism does not excrete fixed quantities of a drug in a unit of time but quantities that vary with the amount present in the body at any one time.

Since a drug after entering the circulation is distributed to the various organs of the body, it may act upon these organs, and it is well to refer to the detectable results as the *Effects*. A very common mistake is to focus attention too closely on a given *Effect* without realizing the numerous combinations of action that may give rise to it. Thus a fall in the blood-pressure is an *Effect* that may be due to such factors as a stimulation of the vasodilator fibers of the sympathetic nerves (dilute solutions of adrenalin), direct depression of the arterioles (the nitrites), injury of the capillaries (the metals), depression of the heart (ephedrine), or to a combination of these factors. Superficially the effects of two drugs may appear the same, yet their seat of action and mode of action may be very different. The excessive optimism that usually attends the introduction of a new drug which appears to produce certain desirable effects, usually precedes the careful pharmocologic and clinical investigation of the mode of action. For example, the physician learns with interest that a new guanidine derivative, synthalin, has been discovered which reduces the blood sugar after oral administration, but he must take an altogether different view of its clinical usefulness when further work shows that its mode of action may be partly through an injury of the parenchyma of the liver rather than through an increase in the capacity of the body to burn sugar. The unfortunate circumstance is that these substances become widely used clinically before such knowledge is available and continue to be used by the physician long after the new facts have been uncovered. It is necessary to emphasize the fact that the *Effects* noted from the use of any drug may result from one of several actions, some of which may be beneficial and others injurious, and it is well to refrain from the use of any drug until suitable scientific evidence is available regarding its seat and mode of action. To analyze the evidence bearing on the

value of a new drug in every case is an exceedingly difficult matter. Few physicians have sufficient chemical and pharmacological training to form a competent estimate from the voluminous literature. We shall presently discuss the sources of information that offer invaluable aid to the physician in his efforts to practice rational drug therapy in the maze of chemical and pharmaceutical production.

DOSAGE

The problem of dosage is a great stumbling-block to the successful use of drugs. The chapters on dosage in most text-books deal with such factors as age, weight, sex, and idiosyncrasy as modifying the amount of the drug to be given. Precision in dosage is believed to be obtained if the substance is accurately weighed or measured. It is the common practice to refer to the dosage of a drug in terms of weight or measure rather than in terms of activity, or in terms of the effects that are to be produced. To commit to memory large tables of dosage, required of the medical student of the past, is not only a waste of time, but actually damaging to the development of a proper point of view. It is not commonly appreciated how little one knows of the actual dose for a given patient when one knows the average, single, approximate dose, for the simple reason that there are no average patients. A knowledge of the average single dose of a drug has *undoubtedly* some value but from it one can no more predict the necessary dosage for a given individual than one can, from the average course of rheumatic fever, predict the exact course of the disease in any given patient. The dose of a drug is not to be looked upon as a relatively fixed quantity that exerts variable actions but rather as a variable quantity that exerts relatively fixed actions.

To the casual listener these remarks may seem like platitudes, and it is perfectly true that in specific instances, this idea is applied almost subconsciously in the treatment of disease, but I venture to say that few physicians apply this principle widely in their use of drugs. We all know that it is irrational to refer to the dose of insulin as a given number of cubic centimeters because the strength of insulin solutions varies and the more severe diabetes requires the larger doses. Yet the very ones who know these facts will not hesitate to digitalize all their patients with two minims of digitalis

per pound of body weight without the slightest regard for the fact that digitalis preparations vary in strength and that patients with more severe heart-failure require the larger doses. I was recently consulted by a physician because, after he had given a patient a daily dose of four and one-half grains of digitalis for about three weeks, he found himself uncertain as to the next procedure when at the end of that time only moderate improvement had occurred and no toxic symptoms were present, although the total quantity had exceeded considerably the dosage determined by an accepted method of calculation which also allowed for supposed daily excretion. If one wishes to know whether a patient has had too much or too little of a drug one does not examine a table of dosage but the criteria of full therapeutic or minor toxic symptoms, both of which are very inadequately treated in most text-books and teaching. The thought I wish to emphasize is that no patients should be considered as having been adequately treated with a drug unless wherever feasible, the full therapeutic effects have been obtained or minor toxic symptoms have been produced. I say "wherever feasible" because there are instances in which experience has fixed the outer limits of dosage which are dangerous to exceed even though minor toxic symptoms have not appeared, as for example, the arsphenamines in the treatment of syphilis. Nevertheless in many instances drugs remain dangerous or very ineffective agents because we fail to use them in that way. If one undertakes to relieve intestinal spasm by atropine, the recommendation to use 1/100 grain two or three times daily is merely a starting point. Increase the dose or repeat it until sufficient drug accumulates in the body to relieve the cramps, or until side actions or minor toxic symptoms (excessive dryness or visual disturbances) appear which preclude the further exhibition of the drug or require that smaller doses be used. It is only then that one knows that the therapeutic possibilities of that drug for that patient have been exhausted. One often sees that three or four different preparations of digitalis have been employed for a cardiac patient and all without success. This shifting from one preparation to another often results from the application of a wrong principle of dosage, namely, that of the relatively fixed quantity without regards to the effects produced. If instead of several different preparations of digitalis only one had been used in this patient, and the

dosage gradually increased until either therapeutic effects had been obtained or minor toxic symptoms resulted, there would have been no need for the use of any other preparation. The manufacturer of scillaren advocates the use of the latter "Where digitalis or strophanthus fails to act." This is a favorite type of advertisement. The fact however is that scillaren will be successful in cases in which digitalis has failed only if the latter has been used in insufficient dosage. It is well to fix firmly in mind the two levels of action of potent drugs; the first (full therapeutic effects) represents the level of action that is desired; the second (minor toxic effects) sets the limits of the therapeutic possibilities of the drug in that patient, and if the desired effects have not been obtained earlier, it marks the point beyond which the drug should not be increased.

The use of drugs with the view of obtaining full therapeutic effects involves as a rule relatively large total quantities and this in turn involves relatively greater dangers. The total quantities however are not given in a single dose except in extraordinary cases. The usual procedure is to build up a level of dosage in the body gradually until such a level is reached at which the full therapeutic effects are produced. If we discontinue a drug before either of the two results are obtained (full therapeutic effects or minor toxic symptoms) we are not justified in speaking of the drug as having failed but rather that our technic was faulty. The dangers can be reduced to a minimum not by merely knowing the average recommended dosage, nor even the average maximum dosage, but by having a *working familiarity* with those signs and symptoms that indicate that no greater therapeutic effects are possible. Drugs cannot be used effectively and safely without confidence in the ability to recognize when a drug can do no further good or when it has begun to do harm. This method makes great demands upon our knowledge; we must know how fast a single dose is absorbed, how long its effects last, how to recognize the full effects, how to recognize the first appearance of toxic symptoms. This procedure makes the use of drugs much more difficult but on the other hand, it is certain to increase by many times the range of successful treatment.

There are few general principles in therapeutics that one can state safely without some qualification. The use of drugs with the view of exhausting the therapeutic possibilities in any given

case is a procedure that can be applied with safety only in the case of those drugs about the actions of which sufficient knowledge is available. Even then it is much safer in the case of some drugs than in that of others. In those cases in which minor toxic symptoms occur relatively early in the course of their action, as in digitalis, this plan can be pursued with little danger. With a drug like cinchophen however, this procedure is attended by greater dangers because occasionally no toxic symptoms occur until the liver has been seriously injured.

To determine dosage in an individual case by the effects rather than by reliance upon average figures is of course not a new idea. It has always been applied almost subconsciously in the use of volatile anesthetics, for example, such as ether or chloroform. One so seldom thinks of the dose of ether for anesthesia in terms of a quantity that very few could probably state with any degree of accuracy the average anesthetic dose of ether. The anesthetist is simply directed to give as much ether as may be necessary to produce certain effects and the skilful anesthetist pays little regard to the quantity used but is thoroughly familiar with the signs of full therapeutic (surgical anesthesia) and minor toxic effects. In a text-book on therapeutics written about twenty years ago this statement is found: "In using digitalis in conditions of any great seriousness the physician should be guided as to the quantity only by the effects." It is necessary to extend that idea of obtaining the correct dose from "conditions of great seriousness" to all conditions in which digitalis is used; and to extend it further from digitalis to all drugs in which that procedure is feasible.

MIXTURES AND THE FORMULARY

This brings us to another matter of great importance, namely, that of the use of mixtures. I do not refer here to the old shotgun prescription. There are still some remnants of it here and there but few people would be willing in this day to admit writing shotgun prescriptions. It is necessary however, to give some thought to the indiscriminate use of mixtures that are generally considered respectable and would not be classed with the shotgun type. One cannot risk using a drug to the point of full therapeutic effects if it is administered in a fixed mixture with other potent ingredients.

For example, one cannot use digitalis to full advantage in the treatment of cardiac failure if each dose also contains some strychnine and caffein in such mixtures as are commonly prescribed. It might be a plausible argument that the caffein might intensify the action of digitalis. The trouble is however that the exact dose of each of the drugs for any patient is not known and that the total quantity of each that is necessary to produce the full effects has to be determined in every case by a gradual increase in the dosage. The full effects for one drug may be reached long before those for the other, so that giving one of the ingredients of the mixture to the full effects, may result in an insufficient or excessive dose of the other. The usual outcome of the practice of prescribing such mixtures is that none of the drugs in the mixture is used in adequate dosage. A rational procedure in a case like this would be to obtain all the effects possible from digitalis first and then if it is deemed desirable, to give the caffein subsequently to ascertain if any additional effects can be obtained by the full dosage of the latter.

Various mixtures consisting of an antipyretic analgesic and an hypnotic of the barbital type (allonal, veramon) are used extensively for the relief of pain. It has recently been shown that the analgesic is much more rapidly eliminated than the hypnotic, hence these drugs should be given separately and not in mixtures of fixed proportions because the dose of the analgesic would naturally require more frequent repetition than that of the hypnotic. It is obvious that the use of fixed mixtures consisting of drugs of widely different rates of elimination results in progressively altered ratios of the concentrations of the separate constituents in the body upon repetition of the dose.

The conventional formulary has little practical value in the practice of rational drug therapy. In these "anthologies" innumerable drugs are juggled and thrown together into mixtures mostly without a semblance of justification, thereby making it impossible to use any of the ingredients to full advantage. Mixtures (for systemic administration) can rarely be employed successfully if we pursue the plan of determining the dosage for every patient in terms of effects, and if we administer potent drugs wherever possible until full therapeutic actions are produced or minor toxic symptoms appear.

EVALUATION OF THERAPEUTIC AGENTS

The modern movement in the direction of rational drug therapy did not begin with a clear slate but with a vast heritage of empiricism. This has made the task exceedingly difficult, especially because the exigencies of practice are such as to promote misconceptions and to foster therapeutic prejudices even in the minds of practitioners of otherwise excellent judgment. The study of the life history of diseases and symptoms without treatment is of course the condition *sine qua non* for a knowledge of the action of any drug in man. This is simply another way of expressing the idea of "control." No single principle in therapeutics is better recognized than that suitable control is the very basis of accurate deductions from the changes that occur in patients after the administration of any drug, yet no principle is perhaps more imperfectly applied in actual practice. It is often impossible for one to appreciate the magnitude of the problem of proper control in fields in which one has not done special investigation. For example, those who have not made a special study of diabetes or hypertension can hardly appreciate the multitude of factors that need to be checked and controlled before the value of a drug in these conditions can be ascertained.

The comparative study and evaluation of most therapeutic agents in the course of private practice are virtually impossible because adequate controls can rarely be obtained. In a case of hypertension it is not usually feasible—though it is quite justifiable—to have a patient make ten or more office visits without any treatment in order to ascertain the spontaneous variations in that patient's blood-pressure, yet unless that is done one can rarely draw any conclusions about the action of a drug upon the blood-pressure with any assurance that the change was not entirely independent of the drug. Few men who have been engaged in research have escaped the experience of at some time having had an hypothesis confirmed by the first few experiments only to have it overthrown by the subsequent course of the work. Those engaged in research often become extreme skeptics because they realize how perilously close to serious blunders they have at times been led by inadequate experiments, insufficient controls, or unsuspected sources of error. Those who have been

engaged in the systematic, painstaking and well-controlled studies of the actions of drugs cannot escape the conviction that the extraordinary, spontaneous variability in the symptoms and signs of disease forms the mainspring of fallacious deductions in therapeutics. The great mass of therapeutic fiascos have their origin in a few seemingly brilliant results in a few badly controlled cases.

That no physician is qualified to undertake the chemical, pharmacologic, and clinical studies that are necessary in order to ascertain the true value of any drug may be generally conceded. But, as I have already indicated, it is also important to bear in mind that few physicians can be expected to analyze the voluminous literature on the various drugs in the detail that is necessary to form reliable judgment from the work of others. The most unfortunate outgrowth of these difficulties is the willingness on the part of many physicians to make an empirical trial of almost any substance or therapeutic procedure that an interested commercial concern or detail man will suggest. The success in this attempted short-cut to the appraisal of new medicinal agents is strictly analogous to that of the inexperienced speculator who, in making a dash for wealth by buying anything a broker recommends, is unfortunate enough to have encouraging results at the start.

The careful study in private practice of the response of patients to a drug in so far as that is possible, even if such studies cannot be suitably controlled, in order to formulate some estimate of the drug from personal experience, is unquestionably of considerable value. But I devote so much time to this point because I believe that one of the greatest obstacles to progress in rational drug therapy is the physician's unwarranted confidence in his qualifications to form an accurate appraisal of the therapeutic merits of a drug under the average conditions of medical practice.

The subject of drug therapy has become altogether too large for physicians to deal individually with the various phases of it. The American Medical Association established the Council on Pharmacy and Chemistry about twenty-five years ago, the primary purpose of which is to help the physician practice rational therapeutics. Most physicians have heard of the Council but few are sufficiently familiar with its personnel, its *modus operandi*, its policies, and accomplishments. It is composed of a group of leaders in chemistry,

pharmacology, and the special fields of clinical medicine with af-
filiations with the greatest medical colleges and hospital organiza-
tions in the United States with enormous facilities for the analyses
and investigation of therapeutic agents both upon animals and man.
Among its various other activities the Council publishes two of the
most valuable aids in therapeutics that are available to the physician
in this country, the book on "Useful Drugs" dealing mainly with
non-proprietary drugs, and "New and Non-official Remedies" dealing
mainly with proprietary substances.

No better illustration can be obtained of the fact that in the
present day entirely different factors dominate the conception of
drug therapy than in the contrast between the size of the old dis-
pensatory and the new book on "Useful Drugs." In the old dis-
pensatory which was the physician's reference book on drugs, about
20,000 articles are referred to or described. By the careful selection
and exclusion of substances that have proved by the best scientific
and clinical criteria to be superfluous or useless, the number of
articles have been reduced to about 450. In other words, only
about two per cent. of the articles in the old dispensatory are re-
garded as essential drugs by the outstanding authorities in medicine
at the present time. There are still many larger text-books in
materia medica, pharmacology, and therapeutics loaded down with
descriptions of innumerable obscure substances of supposed ther-
apeutic merits. A few examples may be cited. The extract of the
prepucial glands of the beaver together with iron, quinine and zinc
valerate, are found in a prescription for "anemia with nervousness."
The infusion of scoparius is given for dropsy in "cardiac weakness
with renal congestion." Cimicifuga is prescribed for "cardiac
asthenia." A prescription containing leptandra, euonymus, ex-
tract of chirata, and podophyllin, is given for "biliousness with
chronic or subacute hepatic torpor." The source of these prescrip-
tions is not an ancient manuscript of historical interest as one
may perhaps suspect, but the last edition (1927) of a popular
formulary. The author expresses a desire there to ,discourage the
use of "proprietary, secret and patented preparations" and states
that "a critical study has been given to each formula in all its parts
and there has been a constant endeavor to summarize the best
therapeutics of to-day." He lists about 800 drugs in about 2,000

prescriptions and refers to them as representing the "collective experience of the profession."

There is an old adage that the average man makes the same mistake a thousand times and calls it experience. No one can deny the importance of clinical knowledge that comes from direct contact with the patient and the actual management of disease, but much of the "collective experience" represented in such works as these serves merely to perpetuate part of our heritage from the days of therapeutic barbarism from which we can emerge only by the careful selection of drugs on the basis of clinical and scientific *Evidence*, rather than on that of testimonials, impressions, and prejudices which unfortunately make up far too great a part of so-called clinical experience in drug therapy.

Scientific clinical *Evidence* is a term with no fixed meaning. Its implications are often ill understood and very imperfectly applied. There can be little question however, that the book called "Useful Drugs" represents one of the most successful efforts in the application of the principle of the selection of drugs on the basis of *Evidence*. This little book lists practically all that one needs in the practice of sound therapeutics, and it is safe to say that the physician of the present day will never be so well off from the standpoint of his knowledge of therapeutics and his success in treatment as when he will confine his selection of drugs with only few exceptions to those non-proprietary substances described in "Useful Drugs."

"New and Non-official Remedies" does not deal so much with those drugs about which the physician reads in the larger text-books but which reach his attention in the form of advertisements in medical journals, circulars, letters and pamphlets. It deals with the proprietary medicine problem. Many of you have never heard of the infusion of scoparius, and though it has had a place in text-books for many decades, most of you, I dare say, do not use it in your practice. But suppose it was brought to your attention two or three times a week by attractive circulars with generous samples and even more generous claims of therapeutic merits, it is very probable that many of you would soon be tempted to give it a clinical trial. It is this practice that makes the proprietary medicine problem so serious and such a difficult one to deal with.

Most of the products described in "New and Non-official Remedies" are not found in the book on "Useful Drugs." This of course indicates that most of the new remedies are non-essential, which is indeed the case. Many physicians fail to consider the fact that a preparation that is new is not necessarily superior therapeutically to older preparations of the same drug. The fashion in drug therapy often changes very much like the fashion in gowns and unfortunately for similar reasons. "New and Non-official Remedies" describes about twenty or more preparations of digitalis although not a single one has the slightest advantage over the official digitalis and most of them cost twenty to 200 times as much. In the text of "New and Non-official Remedies" the following statement is found: "It may be said at once that there is no proof that any of these proprietary preparations can be used to greater advantage than digitalis and its galenicals in the majority of cases of cardiac disease." The Council therefore does not recommend these preparations. What sort of recognition then, do they receive when they are "Council accepted"? When the physician receives these hundreds and thousands of advertisements of new patent medicines only the most gullible will assume the claims to be true. Those who have given any thought to the proprietary medicine question will of course accept no claim as true until satisfactory proof is furnished. To obtain this the physician can go back to the original literature which may be voluminous, confusing, and frequently much of it is in foreign languages which the average physician does not read, or he might ignore much of this and proceed directly to examine the substance clinically. As I have already tried to show, both of these procedures are very apt to result in extremely faulty judgment. A much safer procedure is to refer to "New and Non-official Remedies." If the new drug is not described there or is found in the list of preparations considered but rejected, one can rest assured that the claims made for that preparation have not been substantiated by evidence that can be considered satisfactory to authorities on that subject. There are some exceptions in which preparations are rejected because they fail in other respects to comply with the rules of the Council.

It is a great advantage to manufacturers to have their product accepted by the Council on Pharmacy and Chemistry because that permits them to advertise it in the *Journal of the American Medical*

Association. If a manufacturer fails to submit a proprietory product to the Council it is very probable that he is aware of the fact that the evidence upon which the claims are based is far too tenuous to survive the critical investigation of the Council.

When a new preparation is submitted, the Council makes a careful analysis of the evidence presented to support the claims. The character of the investigation varies with the nature of the product and the claims that are made. In many cases chemical analyses are performed and pharmacological and clinical studies carried out by disinterested workers under the auspices of the Council for the purpose of checking the evidence. In most instances it becomes necessary for the manufacturer to reduce his claims to conform with the results of these additional investigations, the findings of which are usually far less optimistic than the original claims.

When a substance is accepted by the Council it is not on the basis of any superior merit necessarily, though it may possess considerable therapeutic merits, but on the basis of the fact that the claims made for the drug can be substantiated by the available evidence. It is necessary to call attention to the fact that if a product is advertised as having been accepted by the Council, it is well to read the Council report in "New and Non-official Remedies" very carefully, and not to rely solely on the manufacturer's statements which may be strictly true and yet misleading.

The Council makes every effort to guard against the wrong impression being conveyed in the advertisements of the manufacturer after a product has been accepted, but occasionally this is unavoidable. For example, the manufacturer makes the claims that metrazol is capable of raising the blood-pressure and stimulating respiration. These claims are fairly conservative and supported by what appears to be satisfactory evidence; hence, the product has been accepted by the Council. It is left to the physician's own judgment however, to decide whether the product is at all useful in his practice in view of the fact that its action is uncertain, it may reduce the amplitude of the cardiac contraction, and that doses close to the convulsive may be necessary to produce circulatory stimulation. These additional facts are not stated in the advertising

circulars but are found in the description of the substance in "New and Non-official Remedies."

I wish again to emphasize that the Council does not dictate to the physician what he is to use in his practice. It does not even necessarily recommend those products which it accepts. The Council by means of "New and Non-official Remedies" merely aids the physician in doing what he is trying to do himself but without adequate facilities, namely, it helps the physician to divide the great mass of patent medicines into two fundamental classes, those with claims that are valid and those with claims that cannot be substantiated.

Many physicians seem to be unable to resist the temptation of giving proprietary substances a clinical trial even though they may have no other information about them than the manufacturer's fantastic claims and masked testimonials.* A few seemingly satis-factory results in a few badly controlled cases with one of these preparations often produces a conviction of its merits in the mind of the physician that totally suppresses critical judgment. To those who are interested in practicing and promoting rational drug therapy it can only be repeated that "New and Non-official Remedies" is an invaluable guide to the selection of proprietary drugs and that a physician cannot afford to give any consideration to any new drug that is not "accepted." Would any of your patients ever have suf-fered if you had never prescribed a proprietary medicine that was not acceptable to the Council?

DIURETICS

Notable progress has been made in the past few years in the drug treatment of edema. More than one-half of the patients with cardiac edema who fail to respond to digitalis can be very effectively relieved of the water retention by the more effective use of older diuretics or by suitable combinations of the newer ones. A patient with luetic heart-disease developing congestive heart-failure with edema, ascites, and hydrothorax who showed little or no improve-ment after full digitalization required tapping at intervals of three to six months. Such a patient receives altogether different treatment

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* These are frequently reprints of articles that pretend to be results of investigations but which in fact give no evidence of scientific method.

today. With suitable doses of the newer diuretics he loses forty to fifty pounds of edema fluid in a week or two, and in three or four weeks is ready for discharge from the hospital with therapeutic results far more complete than were possible in the days before this treatment was available. Furthermore, the mechanism of the diuretic action is viewed from a somewhat different angle. The extrarenal factor in the action of certain diuretics is receiving a great deal of emphasis, namely, the fact that some of these diuretics do not produce their effect by increasing the blood flow through the kidney (as a primary action) nor by any other direct action upon the kidney but by changing the physical or chemical state of the blood or tissues so that retained fluids will be liberated and made available for excretion by the kidney. There are still many obscure factors in our knowledge of the mechanism of diuresis as there are in that of the mechanism of retention of urinary constituents. Numerous observations are, however, accumulating on the relation of the inorganic constituents of the blood and tissues to the retention of fluids and the diuretic action and while there is not sufficient knowledge for a complete correlation many of them are extremely interesting and important from the practical standpoint, as for example, the loss of effectiveness of novasurol with the fall in blood chlorides and the restoration of its effectiveness with the restoration of the blood chloride level.

Novasurol. The value of mercury in various forms for increasing the secretion of urine has been known for centuries in clinical practice. As early as 1799 Ferriar recommended calomel for increasing the diuretic action of digitalis. Nearly one hundred years later Jendrassik called attention to the striking diuretic effects of repeated small doses of calomel in patients with edema. Numerous reports of kidney injury by various observers discouraged the use of all forms of mercury as diuretics and the vogue for these substances practically disappeared.

The use of mercury as a diuretic has again come into prominence in the past ten years through the introduction of novasurol by Saxl and Heilig in 1920. Novasurol is a complex organic compound of mercury in combination with veronal. It was first introduced for the treatment of syphilis but its marked diuretic action has attracted far more attention. Novasurol is supplied in solutions

containing 10 per cent. of the drug which in turn contains about 30 per cent. of metallic mercury (approximately one-half grain mercury in each cubic centimeter of novasurol solution). When novasurol is injected in a patient with edema there occurs within one to three hours a marked increase in urine flow which reaches its maximum in six to eight hours and terminates in about twenty-four hours. The most striking change in the solid constituents of the urine is the marked increase in the secretion of chlorides and fixed base (particularly sodium) both in total quantity and concentration.

The usual dose is one to two cubic centimeters injected intramuscularly. It may be given intravenously but there is no particular advantage since the action comes on practically as quickly after the intramuscular injection. Great care must be exercised not to inject it subcutaneously because of the danger of local irritation and necrosis of the tissue at the site of injection. Some recommend that the dose be repeated not more frequently than at four-day intervals. It may be repeated every other day or even daily for short periods of time. Too frequent repetition occasionally causes diminution of the urine output as the result of kidney injury.

This drug is most effective in edema of cardiac failure, and is effective when digitalis and other diuretics have failed. It is to be avoided in the edema of renal disease because of the possibility of increasing the renal damage. The following toxic symptoms may arise which preclude the further use of the drug: albuminuria, stomatitis, vomiting, bloody diarrhea. When the drug is properly given these symptoms are rare. It is well to begin with a very small dose to determine excessive susceptibility to the action of mercury.

Acid-forming Diuretics. The chemical aspects of the diuretic action are well illustrated by the action of substances known as the acid-forming salts—calcium chloride, magnesium sulphate, ammonium sulphate, ammonium chloride, and ammonium nitrate. When these are introduced into the body in large quantities they produce signs of acidosis (diminished CO_2 combining power of the plasma, increased excretion of ammonia, increased excretion of chlorides and fixed base in the urine). It has been found that increased acidity of the blood (shift of the buffer system to the acid

side) favors the movement of water in the direction of the kidneys. This fact is related to the observation that sodium and water metabolism are interdependent—the storage of sodium in the tissues favors the accumulation of water, and that increased acidity lowers the base binding capacity of proteins.

Ammonium chloride is the most popular member of this group. It is employed in very large doses, five to twenty grams daily, given orally and well diluted. The ammonia is rapidly converted into urea with an increase in the blood urea and urea excretion in the urine. The chloride ion that is liberated increases the acidity of the blood, although there is some evidence that the specific action of the chloride ion as well as the relation of other ions in the body play a part in the diuretic action of the salt. This accounts for the fact that occasionally even in the presence of marked acidosis diuresis may be slight or absent. Besides the gastric symptoms from local action, symptoms of acidosis set the outer limits of dosage.

A very striking characteristic of the diuresis by ammonium chloride is the marked increase in the urinary chlorides and fixed base. Like novasurol, ammonium chloride is most effective in the edema of cardiac origin. In certain cases a combination of the two will produce results not obtainable with either alone.

I have referred to the more effective use of older diuretics. Inadequate dosage is partly responsible for the failure to obtain more satisfactory results. It has recently been shown (Goldring) that more than one-half the patients with cardiac edema that fail to respond to digitalis, improve after theophylline (theocine) in doses of nine to thirty grains daily. Urea was introduced as a diuretic about forty years ago and favorable results were obtained, yet the substance fell into disuse partly because of theories concerning the relation between urea and uremia. In recent years urea has again acquired a place as an effective diuretic in both cardiac and nephritic edemas. It is given in large doses of thirty to one hundred grams daily. It has a disagreeable metallic taste, hence should be given well diluted and after meals to avoid gastric disturbances. The only toxic symptoms that occasionally arise are weakness and drowsiness in association with excessively high-blood urea. These symptoms disappear in

a day or two after the drug is discontinued. There is no evidence of injury to the kidney.

The substances that depress the central nervous system and induce sleep have a wide field of usefulness in therapeutics. Since veronal was introduced about thirty years ago a large number of barbituric acid derivatives have appeared on the market, such as dial, medinal, luminal, ipral, phanodorn, amytal. Efforts have been made mainly by manufacturing chemists to modify the chemical structure of these substances so as to diminish their toxicity and enhance their hypnotic and analgesic properties. The claims made at the outset are usually based upon the results of animal experiments and are of two kinds; first, that the new preparation is more effective therapeutically, and second, that it is safer than veronal. It is a very striking fact that the pharmacologic differences between the various members of this group of drugs that are in evidence from experimental work carried out by the manufacturer, practically always disappear when similar experiments are carried out by disinterested workers and in such a way as to make the identity of the drug unknown to the experimenter until the interpretation of the results has been recorded. Those familiar with the behavior of animals toward the barbituric acid compounds are familiar with the numerous difficulties that beset a precise comparison of their actions. These tend to vitiate the results, and unless care is taken to exclude subjective factors by the "blind test" it is difficult to avoid totally erroneous conclusions.

The margin of safety is the ratio between the minimal effective or hypnotic dose and the minimal toxic or fatal dose. It is obviously impossible to carry out such determinations in man with any degree of precision. It appears to be fairly certain from animal experiments, however, that the therapeutic and the toxic actions of the various members of this group run essentially parallel, and that whenever the chemical structure of the barbituric acid has been changed so as to increase the hypnotic action, the intensity of the toxic action has been increased to practically the same degree. When physicians find that one member of the group has proved to be a more effective hypnotic than the other in their practice it is

because they have not made strictly comparable observations. For example, amytal is supplied to physicians in one and one-half grain tablets with the directions to prescribe one or two tablets before bedtime. Since amytal is about four times as toxic as veronal two amytal tablets are equivalent in potency to about twelve grains of veronal. It is not common to prescribe twelve grains of veronal in a single dose yet physicians will commonly prescribe three grains of amytal without the knowledge that these two doses are strictly equivalent in toxicity. The Council makes these analyses and comparisons and does not accept these hypnotics for "New and Non-official Remedies" as long as unsupported claims for relatively greater effectiveness and safety are made. It is important to bear in mind that if one gives the various members of this group of drugs in comparable doses, not in terms of tablets or grains, but in terms of their relative potency, it will be seen that they all have approximately the same safety and therapeutic efficiency.

THE FIXED ANESTHETICS

The volatile anesthetics give us a great deal of trouble. There is difficulty in maintaining a constant anesthesia during the operation; there is nervousness and struggling during the period of induction; gastro-intestinal symptoms during the period of recovery; and many patients develop postoperative pneumonia. These and other difficulties have given impetus to the search for fixed anesthetics. The various hypnotics—the barbituric acid derivatives and others—have been recommended for this purpose at various times during the past twenty-five years or longer. They have never become very popular anesthetics except in the animal laboratory in which case a one or two per cent. mortality from anesthesia alone is not considered very serious. We are now passing through another period of very active propaganda for the use of fixed anesthesia in man.

It would be well to consider for a moment the physiologic conditions that attend the production of general anesthesia. There is profound depression of the brain, the spinal cord and the reflexes. The only portions of the central nervous system that remain active are the vital centers in the medulla. There is no single instance in drug action in which such profound and generalized depression is aimed at as in the production of general anesthesia. There cer-

tainly are few if any instances in drug action in which the margin between therapeutic (surgical anesthesia) and fatal doses is so small as in the production of general anesthesia.

Patients show great differences in their susceptibility to all drugs and where the full effects are aimed at, overdosage in a fair proportion of cases is inevitable. We do not ordinarily think of ether anesthesia as particularly dangerous and we rarely become alarmed at signs of overdosage because of the ease with which they can be overcome by a few deep respirations. It is well known that the shock of operation also modifies the susceptibility to the anesthetics and a quantity that may be harmless to the normal patient may prove injurious when shock factors are added; hence, what is a necessary dose at the beginning may become an overdose in the course of the operation. We rarely give much thought to this fact either, in the case of the volatile anesthetics because we diminish or increase the depth of anesthesia almost subconsciously, depending upon the condition of the patient.

There is therefore a fundamental objection to the use of a general anesthetic which cannot be eliminated through the lungs in a few minutes but requires several hours for excretion through the liver or kidneys. The primary issues are obscured by those who recommend the general use of such drugs as barbital (veronal), amytal or avertin for anesthesia in man. The question is not which is safer than another, but whether the production of general narcosis by a non-volatile anesthetic is not in itself a very dangerous and unwarranted procedure. When it is stated that as much as twenty-two grains of amytal is injected intravenously into a patient for general anesthesia, one can only appreciate the full significance of that procedure when one realizes that that dose is the equivalent of about 130 grains of veronal.

These substances for fixed general anesthesia come and go in waves of popularity. They all have a very similar history. They are introduced for the production of general anesthesia with claims of absolute safety. As the reports of deaths begin to appear a change in the preparation of the substance (usually of minor importance) is announced by the manufacturer for diminishing the toxicity. After more accidents are reported they begin to recommend smaller doses, and when the doses become safe they also become ineffective

for general anesthesia. Soon one finds the substance no longer exploited as a general anesthetic but in combination with other depressants to supplement the volatile anesthetics. The unfortunate circumstance is that these substances do not die a natural death but from the force of experience in which many patients are sacrificed. At the present time a fixed anesthetic known as avertin is being promoted very energetically in this country though the foreign literature contains numerous reports of fatalities.

<div align="center">CAMPHOR</div>

Belief in the efficacy of camphor as a circulatory stimulant is mainly of continental importation. Camphor, however, has gained a very firm hold upon the popular imagination in this country also and the average emergency kit is rarely without an ampule of this drug. Its reputation has not suffered so much as it might have because of the fact that it is usually recommended in emergency conditions in which control observations are practically impossible. There are scores of papers in the literature dealing with the experimental aspects of camphor action in various animals and very striking effects are observed on the respiration, the heart and the blood-pressure. This is a good example of the discrepancy between experimental and clinical evidence. Excessively optimistic conclusions from animal experiments have helped to create a clinical reputation for a drug that careful clinical observations cannot justify. There have been several carefully controlled studies of the action of camphor in this country in groups of patients with objective and measurable signs of heart-failure and respiratory disturbances, in which not the slightest evidence of beneficial effects resulted. Varying doses were used, from five to thirty grains dissolved in oil, injected subcutaneously or intramuscularly. Doses of about thirty grains were in some cases repeated every two hours for three injections without any signs of beneficial effects. It must be borne in mind that favorable results with camphor are reported only in ill-controlled studies almost without exception, and that studies in which patients were used in whom beneficial results could not escape detection and in which sufficient control observations were made so as to render it possible to distinguish between spontaneous changes and those resulting from the drug, give little ground for the

continuation of the use of camphor in circulatory or respiratory disturbances.

The belief in the value of camphor has stimulated the search for soluble camphor derivatives because camphor is insoluble, and has resulted in the exploitation of such preparations as Cardiazol and Hexeton. To have made camphor soluble makes it possible to inject it intravenously and makes it active in very small doses. It does not improve the substance, however, from the standpoint of the essential objections to camphor, namely, that it exerts a very brief action, that its action is very uncertain, and that doses close to the convulsive are necessary for effective stimulation of the circulation.

The conditions here are analogous to those attending the introduction of alpha-lobelin as a respiratory stimulant. Alpha-lobelin is closely related to nicotine which has long been known to produce very striking respiratory stimulation in experimental animals. As a matter of fact one of the most sensitive tests for nicotine in the laboratory is the intense stimulation of respiration in the frog. Nevertheless, nicotine has proved practically useless as a respiratory stimulant in man and recent scientific work on alpha-lobelin has proved that this drug also gives the physician a false sense of security when relied upon in the treatment of patients in whom respiratory stimulation is necessary; they point out the extreme uncertainty of its action and the dangers of further depressing rather than stimulating the respiratory center when it is already depressed.

POSTERIOR PITUITARY EXTRACTS

Since Oliver and Schafer in 1895 discovered that an extract of the posterior lobe of the pituitary gland raises the blood-pressure, a great deal of pharmacological and chemical work has been done to elucidate further the actions and the composition of these extracts. Most investigations have dealt with the three essential actions of the extracts of the posterior pituitary, namely contraction of the uterus (oxytocic), elevation of the blood-pressure (pressor), and the renal action (diuretic-antidiuretic action).

Many chemical substances have been held responsible for these various actions. In 1919, Abel and his co-workers set forth evidence showing that the three primary actions of the posterior pitui-

tary were all due to one substance many times more potent than histamine. It is hardly necessary to state that it was of considerable practical importance to know whether one or more principles in the extracts of the pituitary produce the various actions because the United States Pharmacopœia only required an oxytocic standard. It is evident that two official pituitary solutions having the same potency in stimulating the uterus would have the same potency in raising the blood-pressure, only if both actions were due to the same substance or to different substances in fixed ratios. Great interest has therefore been aroused by the recent work of Kamm and his collaborators. By chemical manipulation they were able to prepare a pituitary extract that was extremely potent in pressor activity but very weak in oxytocic activity. In repeating the work they found that the fractions which they had previously discarded contained most of the oxytocic activity. They perfected the method of separation of these two substances to the extent of 95 per cent. on a manufacturing scale. They are both prepared in powder form and soluble in water, and are supplied under the names of pitocin and pitressin. Pitocin is sold in ampules containing a solution of which one cubic centimeter represents ten oxytocic units similar to the oxytocic activity of the United States Pharmacopœia pituitary solution. Pitressin is supplied in a similar way except that each cubic centimeter represents twenty pressor units or twice the pressor activity of a cubic centimeter of United States Pharmacopœia pituitary solution.

We have therefore the first time a solution of the uterine stimulating substance of the posterior part of the pituitary that is practically free of the principle which raises blood-pressure, and another solution, of the blood-pressure raising substance practically free of the one that stimulates the uterus. The renal and some of the other actions of the posterior pituitary extracts appear to be associated with the pressor substance (pitressin).

DIGITALIS

The chemistry of therapeutic agents is usually considered as belonging to the realm of preclinical interests rather than as a subject with a direct clinical bearing. It is somewhat different in the case of the digitalis bodies. We see such statements as "purified digitalis," "standardized digitalis," "uniform digitalis." We see

the claim that this or that preparation is protected against deterioration or that it is less irritating to the stomach because of the removal of impurities. Druggists take pride in announcing that they only buy small quantities of a digitalis preparation at a time so as to have a "fresh" supply at all times. These references to the composition and pharmacology of digitalis can have little meaning to those who do not have some understanding of the chemistry of this important group of drugs. This knowledge makes it possible to understand why the scores of proprietary digitalis preparations at costs as high as 1,000 times that of ordinary digitalis, have served only to confuse and bewilder the physician, and have contributed nothing of real merit to the therapeutic use of the drug. Many of the thoroughly controlled studies of the past few years have gone a long way to clarify the situation and to promote much saner views in regard to digitalis therapy. The latter may be summarized very briefly.

Digitalis is composed of a mixture of glucosides and thus far the only glucosides in digitalis that appear to be pure principles are digitoxin, gitalin and bigitalin. All other glucosides (with the digitalis action) obtained from the crude drug are mixtures—digitalien, the digitalins, digalen, digifoline, digitan and the host of other proprietary as well as nonproprietary preparations. All the digitalis glucosides produce the same qualitative digitalis action, hence there is no advantage in the use of any extract of digitalis over the ordinary digitalis leaf, and results that cannot be obtained with digitalis itself, cannot be obtained with any other preparation or other member of the group providing digitalis has been used in adequate dosage. Digitalis leaf shows no appreciable deterioration when kept under ordinary conditions for many years, hence, the claims for special merits on the ground of protection of the digitalis leaf against deterioration, have no justification in fact. "Purified digitalis" usually has no practical meaning because the saponin is the only potent impurity and it is present in an amount that is harmless when taken by mouth, and the amount of other impurities present in the usual doses of digitalis are of the same character as, and of no greater quantity than found in a few leaves of lettuce. The term "standardized digitalis" requires some explanation. The only way that digitalis preparations can be standardized is in terms

of potency. Many have come to believe that "standardized" preparations are uniform. Nothing could be further from the fact. In the first place different manufacturers call their digitalis "standardized" but there are many different standards so that some so-called standardized preparations are as much as twice as potent as others. Even if one uses specimens of the same potency they are not necessarily uniform because different specimens may differ not only in potency but in absorbability and rate of elimination and the latter two factors are not tested by any of the usual methods of standardization. Commercial specimens bearing the same name, even if uniform in potency (many of them are not) are not uniform in other respects (absorbability, rate of excretion) because they are prepared from different lots of the crude drug. The most serious difficulty that the practitioner encounters in the use of digitalis is the uncertainty as to the quality of the drug. When a patient in heart-failure receives comparatively large doses of digitalis or a digitalis proprietary, such as digitan or digalen, and fails to show improvement it would be of inestimable value to the physician to have some assurance that his failure to obtain results is not due to some peculiarity in the potency or absorbability of that specimen of the drug. If a physician gives a patient a daily dose of a digitalis preparation for six months or a year and the patient at the end of this time develops congestive heart-failure or signs of digitalis poisoning, it is not possible to know whether these results are due to a change in the patient's heart or to some unsuspected variations in the different specimens of the drug which he has been compelled to use during that period.

Absolute uniformity (in potency, absorbability, rate of excretion) can only be obtained at the present time by using the same *specimen* of the drug. This formed the basis of a plan for the use of digitalis in the Adult Cardiac Clinic of Bellevue Hospital in 1922. A supply of dried digitalis leaf was obtained sufficient to last several years. It was standardized by the cat method. From time to time parts of this were made up into compressed tablets in terms of cat units (1, 2, and 3 cat units per tablet). It is self-evident that greater precision in dosage was possible by the use of tablets in a single daily dose for the average ambulatory patient than by the use of liquid preparations in terms of drops, minims or teaspoonful doses several times daily. This plan has been further developed by the digitalis

committee of the New York Heart Association (now the Heart Committee of the New York Tuberculosis and Health Association). It has been in successful operation in nearly forty cardiac clinics to whom the association distributes this digitalis at a cost that is less than one-half as much as the cheapest digitalis on the market. The greatest virtue of this plan is that it supplies physicians with truly *uniform* digitalis and it removes the uncertainty as to the quality of the drug which is one of the most serious obstacles to its successful use. Some manufacturers have already undertaken to supply digitalis on a commercial scale in accordance with the general plan adopted by the heart association.

The conception of digitalis dosage has undergone considerable modification in the past few years. It has been shown that patients with heart-failure cannot be considered as a homogeneous group from the standpoint of their need for digitalis and that patients in advanced heart-failure require much larger quantities of digitalis to induce the necessary improvement than the average ambulatory cardiac patient. It has also been shown that the full therapeutic effects of digitalis may be induced in the average ambulatory cardiac patient by the daily repetition of relatively small doses of the drug—from three to six grains daily—varying with different patients and with differences in the potency of the drug and that these same doses may then be continued as the daily maintenance doses without inducing toxic symptoms. This is illustrated in the accompanying diagram. (Fig. 1.) The commonly accepted view that patients excrete about two grains of digitalis daily has been shown to be based upon a misconception, that the amount a patient excretes daily is not a fixed quantity but varies with the amount present in the body.

Fig. 1.
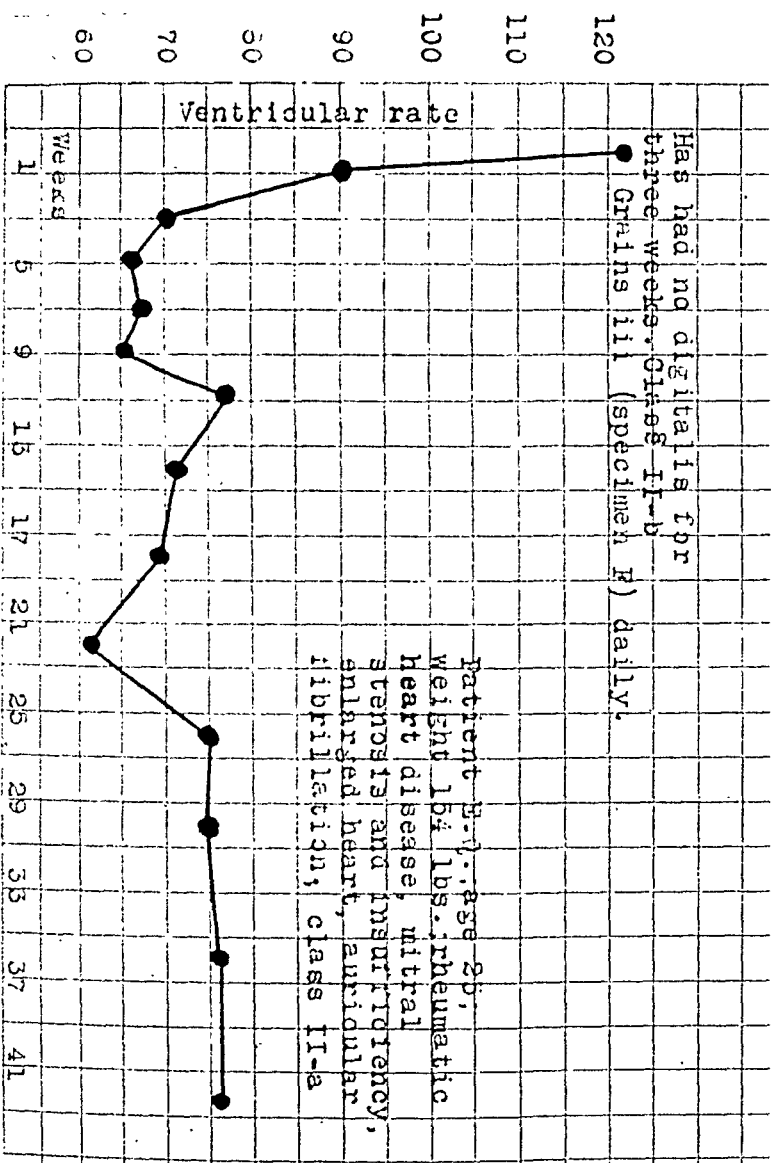
Chart showing the effect of the administration of digitalis on the ventricular rate.

Pædiatric Contributions from The Heckscher Institute for Child Health

CHILD HEALTH

By I. NEWTON KUGELMASS, M.D., Ph.D., Sc.D.

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HEALTHY childhood is a dynamic equilibrium of all internal mechanisms with all external environmental forces. The equilibrium persists from moment to moment, keeping pace with the changing child as a result of life's processes. It is a continuous harmony wherein the activity of any one organ is regulated by all the others to produce a unanimity of biologic function. There are no distinct parts for all are integrated and their activity is indivisible. The child has no intuitive knowledge of the workings of the parts of his body. He is "something happening" continuously.

Disease is a disharmony, a disturbance of the general unified functioning of the body—the indication of truly partial activity. Then, and only then, comes the consciousness to child, parent and physician of a discordance of function revealed by the definite impairment of an organ. The first cause of disease is associated with a single organ, the recognition of which may halt the process and the neglect of which may allow its transmission to other systems of the body. Disease in its initial offense is local, gradually giving way to universality of impairment of life's processes.

The range of life between optimum health and frank disease constitutes the body's buffering mechanism of self-preservation. Body offenses of mechanical nature are guarded against by intuitive ingenuity; those of infectious insult are overcome by immune substances; those of chemical nature are neutralized. And so, as the animal body evolved in the course of eons of time, there developed automatic protective mechanisms specific for the type of insult—all in the cause of self-preservation. As civilized life brings new hazards, so are corresponding internal changes brought to bear in

dire attempt for the maintenance of life. Ancient knowledge was primarily concerned with the types of body offense productive of disease, while modern medicine is more concerned with the methods preventive of such disturbances. Preventive medicine concerned with the growth and development of childhood yields knowledge that will enable a child to be well born, to thrive lustily without halt during infancy, to be able physically, mentally and socially to acquire a sound education, to emerge from difficult adolescence into sound maturity, with the modern physician as guide and mentor..

The physician is gradually coming into his own in the evolution of this industrial era. Thus far, civilization has been built upon governments, institutions, industries, great cities with all the impersonal perfection thereunto belonging. Now we are approaching humanization—the perfection of mankind as well. Markham visualizes the present order of things:

> "We are all blind until we see
> That, in the human plan
> Nothing is worth the watering, if
> It does not make the man;
> Why build these cities glorious
> If man unbuilded goes?
> In vain we build the world
> Unless the builder also grows."

Primitive man had but one hygienic problem—how to fill his stomach. Food-gathering insured him ample outdoor exercise; raw feeding assured abundance of vitamins; housing constituted no difficulties. The prehistoric flint-chipper emerged from antiquity and evolved a housing problem because the cave-space was limited. He retained his happiness, his teeth and his digestion living on fruit, berries and occasional game which could not be stewed for lack of pottery, then unknown.

Primitive communes formed when man learned to build huts, tame animals and till crops, thus requiring a mutuality in work and defense. Settlements began to dot the river-banks and millions passed before survivors at last realized that quality of water was more important than quantity. Finally, after many generations, did

man adopt for disposal of his excreta, the art taught by the dog to Adam a million years ago.

Sanitation was first in evidence during the Minoan Era, 2000 B.C., when in Knossos Palace was installed a system of latrines and drains for the removal of excreta by water-carriage. By 500 B.C. the level of sanitation is reflected in the duties of the Roman "Aedile"—repair of drains, prevention of foul smells, maintenance of good grain, destruction of bad food, supervision of baths, *etc.*

Infant care amongst early races depended very largely upon their religion and the character of their soil. Those under the guidance of matriarchal deity treated their children with kindness while those who worshiped a patriarchal deity murdered their infants at birth, maltreated them or sacrificed them for rituals. But the nature of the soil also contributed greatly to the reaction of these early races to their offspring. Those who lived on fertile soil cared well for their progeny while those who suffered hardship on barren land acted accordingly.

Infanticide, particularly in female babies, has been in vogue in countries like China and India (where economic conditions have been severe and the religion patriarchal in type) until the seventeenth century, when the first official edict was promulgated against such practice. Nevertheless, a fourth of the new-born female infants of China are still being drowned. Female infants are preserved in sufficient numbers for breeding soldiers. Similar practices prevailed amongst the ancient Persians, Carthaginians, Arabs and Phœnicians. With the advent of Christianity and Mohammedanism have these horrors gradually ceased. Infanticide still remains a practice amongst the savage tribes—West African negroes, Polynesians, Papuans, Kaffirs, *etc.* Throughout all ages there have always been great men and women who fought for the preservation of infants and children by advancing sound principles of child health.

Hammurabi, about 2500 B.C., developed a code of laws which gave unusual protection to women and children. Egyptian medical law reveals a system of medicine on the care of infants, written about 1500 B.C. Greek and Roman literature is abundant in references in Gallen, Quintillian and others on child hygiene. Spartan mothers were required to look upon statues of Castor and Pollux in order that they might give birth to strong and beautiful children

for they were reared on the principle of "the survival of the fittest."
New-borns were plunged into a bath of ice-water and those that
survived were fit to be reared.   Hippocrates, 400 B.C., was the
father of paediatrics.   He evolved many standards and practices in
infant hygiene.

The first laws for the protection of infants were made in Rome.
When a baby was born the midwife placed it at the feet of the father,
who was given the power of life and death of his family.   If he
picked it up, it became a member of the family; otherwise, it was
killed.   Caesar abolished the "patria potestas."   Autumeis Pius, in
the second century, rewarded mothers for nursing their babies suc-
cessfully and established institutions for the care of infants.   Arch-
bishop Datheus, of Milan, in 787 established the first asylum for
abandoned infants to be reared by the church.   Since then many
foundling hospitals have been established throughout the world.   In
1523, Hotel-Dieu of Lyons, the oldest hospital in France, admitted
infants and children for medical care.

The first public hospital was established in the Temple of
Aesculapius in the first century A.D.   The duties of the public medi-
cal officers appointed to the hospital were according to the Edict of
Valens: "knowing themselves to be paid for attending the poor, they
must think less of the rich; and, being paid, must take what men
recovered from sickness will give, not what men, fearing for lives,
will offer."   The first children's hospital in Europe was founded in
Paris in 1802 and through the genius of its proponents, Trousseau,
Rodger, Bouchiet and others, it became the great European teaching
center for scientific paediatrics.   The second children's hospital was
established in Russia in 1834.

The fundamental doctrines of preventive paediatrics were pro-
pounded in 1774 by Underwood.   He demonstrated that the health
and welfare of a nation depended upon the care devoted to its infants.
Von Rosenstein was the Swedish pioneer in the art of paediatrics.
He was the first to administer medicines to the mother or wet nurse
whose nurslings were ailing because such medication would be trans-
mitted through the breast milk.   He made syphilitic babies suckle
from the udders of a goat which had been previously treated by
mercurial inunctions, thereby reducing infant mortality.   But the
goat as a wet nurse was by no means an innovation, for, according to

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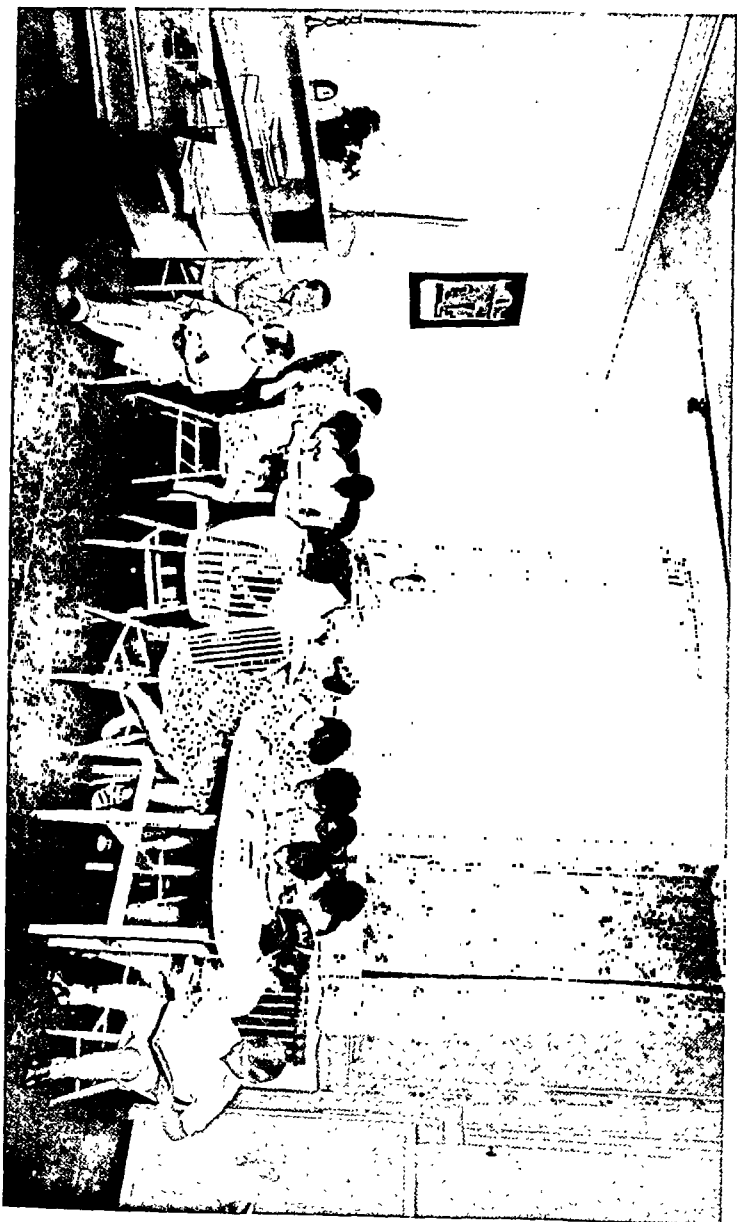
The Nutrition Clinic.

FIG. 2.

FIG. 3.

Laboratory Examination of Potential Problems.
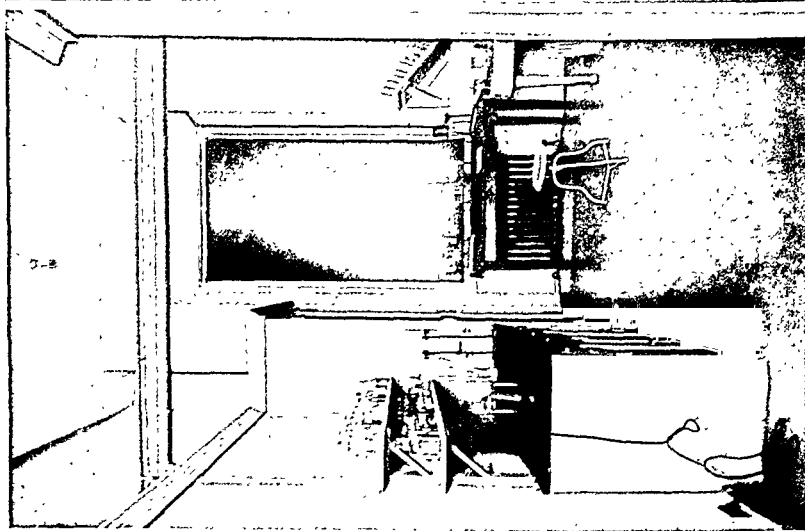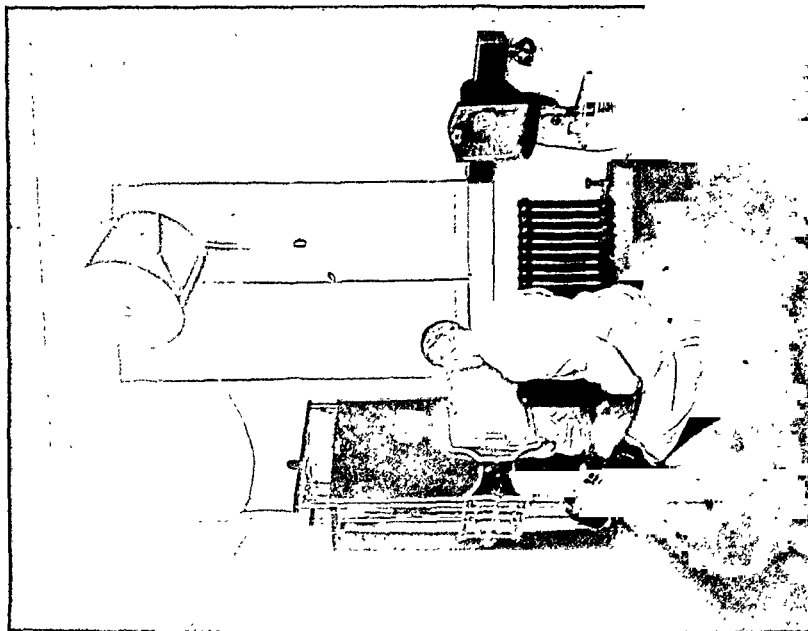
Greek mythology, Aesculapius and Jupiter were suckled by a goat, and Remus and Romulus, of Roman mythology, by a she-wolf, and thus acquired their great physical strength. This practice became widespread throughout France and Germany and still prevails in South America and India as a direct means of artificial feeding without intermediate contamination.

The character of the development of life, *in utero* was first brought to the fore by Ballantyne in 1902, initiating a prenatal clinic for the scientific study devoted to the cause of the perfection of the new-born. Prematurity was fatal until Tarnier introduced incubators into the French maternity hospitals. The eyesight of the new-borns first began to be protected by the installation of silver nitrate into their eyes by Crede in 1844, a mode of treatment which was to some extent practiced by Soranus in the second century. Today this practice is prescribed by law in all civilized countries.

Medical truths appear and reappear. The transmission of typhus fever by the louse was first observed by Tobias Cober, of Gorlitz, in 1606. But the sanitarian is like the old Greek, Cassandra, who had the gift of prophecy, but also the curse that no one would believe her. Percival Pott, in 1779, described what now is known as Pott's disease, but Hippocrates also noted the relation between phthisis and spinal deformity. We prate about our modernity, that there was never anything like it, forgetting the sanitary plumbing of Crete (3400 B.C.). The nineteenth century boasts the relation of the mosquito to malaria but the idea is in Susrata. When we isolate patients with infectious diseases and incinerate the infectious material, we have come as far up in the prevention of disease as Moses. Medical truths are like the flower of the field that is cut down, like the grass that withers, but the root or the seed remains only to spring up again, perhaps again to be trampled under foot unheeded. Galen spoke and the medical world stood still for centuries.

Primitive medicine with its Egyptian and Oriental congeners was essentially a phase of anthropology. Greek medicine was science in the making with Roman medicine as an off-shoot, Byzantium as a cold-storage plant, and Islam as a traveling agent. The result of medieval medicine pertaining to childhood was the organization of hospitals, sick nursing, medical literature and education. The Renaissance contributed surgery; the eighteenth century instrumen-

tal diagnosis, preventive medicine and public hygiene; the nineteenth century organized science and the twentieth is again social.

The philosophy of the past meted out nothing to childhood but a frown of disapproval, while that of today is most tolerant:

"Nothing has a better influence on children than praise."—Sir Philip Sidney. "Where on earth is there so much society as in a beloved child?"—Landor. "Dispel not the happy illusions of child-hood."—Goethe. "Children have more need of models than of critics."—Jourbet. "Do not try to produce an ideal child; it would find unfitness in the world."—Herbert Spencer. "The vilest abortionist is he who attempts to mold a child's character."—Bernard Shaw. "Not one book in a thousand is worth as much to mankind as an innocent little child."—H. L. Mencken.

II

Preventive medicine began in 1798 when Jenner initiated vaccination against smallpox. Infant mortality was thereby materially decreased, but simultaneously this stride was greatly altered by industrial intervention. Industrial development altered the whole trend of life. Factories were located near mines instead of on remote river-banks. Agriculturists flocked to these mushroom centers in quest of quick-won fortunes. Legislators were either too busy or too ignorant to pass public-health laws and so the slums which evolved to house this horde of workers persist to this day. Women were drafted into machine shops from rural districts with neglect of their children and spread of venereal disease.

Continuity of scientific advance in the cause of prevention of disease was made possible by the existence of over a century of valuable scientific instruments, like the microscope in 1620, the thermometer in 1638, *etc.* The search for micro-organisms led to the discovery of the diphtheria bacillus by Klebs, in 1875, which was first grown by Leoffler in 1884 and is now known as the Klebs-Leoffler bacillus. Infectious diseases then began with a very definite micro-organism etiology.

Infectious diseases are due to micro-organisms which have invaded and multiplied in the child's body. Each infectious disease is produced by a specific organism. Some have actually been identified and isolated, as in the case of tuberculosis, diphtheria and

typhoid fever. While in the case of others, like measles, chicken pox, *etc.*, the causative organisms have not been isolated because of their ultra-microscopic natures. Infectious diseases develop in a manner comparable to a plant. They require not only the seed but the soil. A child in good health is less apt to be the recipient of an infectious insult than one in a poor state of health.

Infectious invasion of the body results in germination and multiplication of the organisms. They liberate toxins which are absorbed into the blood-stream, thus giving rise to symptoms of the disease of which they are the specific organism. The animal body reacts to such invasion by having the white blood-cells attack and engulf the microbes. Mechnikoff, in 1884, first observed this phenomenon of phagocytosis. In addition to this protective mechanism specific antitoxins are formed by the reticulo-endothelial system which bring about the child's recovery. In fact, the very presence of these antitoxin bodies in the child's blood retains their immunity to further attacks of the same disease.

Immunity against infection may be either natural or acquired. Some people are naturally immune to certain diseases. Negroes are not susceptible to yellow fever. Mongolians are immune to scarlet fever. Human beings are immune to most animal diseases while animals are not susceptible to most infectious diseases. Acquired immunity is produced by a previous attack of the disease or by frequent exposure to small doses of the organisms insufficient to actually produce the disease but adequate to adjust the body cells to protect themselves against the disease. Vaccination with the organism or its products is a graded means of producing immunity. Passive immunity is temporary, acquired only by direct introduction of antitoxin material into the child's body. New-born babes are protected against infectious disease because of the presence in their blood of the antitoxins which new-borns receive from their mothers.

Acute infectious diseases are transmitted by direct contact. They are only exceptionally seen in infants during the first six months of life because of their passive immunity acquired from the mother, through the placental circulation in intra-uterine life. This immunity disappears by the sixth month and susceptibility to each of these diseases varies with each child. Nearly all children are susceptible to measles, but only certain types of children to infantile paralysis,

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while the susceptibility to scarlet fever ranges somewhere between these two extremes. Heredity determines greatly the degrees of susceptibility as against the intensity of immunity.

The prevention of communicable diseases has been developed to a refinement along two distinct lines: first, by the control of exposure through isolation and quarantine of individuals with the diseases, and, second, by biological methods with the purpose of immunizing susceptible children against a specific infection by means of active and passive immunization. The early methods of fumigation and segregation are of questionable value.

Prevention of diphtheria began with the discovery of the toxin test by Schick and the toxin-antitoxin mixture by Park, in 1915. The combined procedure thus far reduced the number of cases by one-half and the number of deaths by four-fifths. These striking results have become more obvious when infants and pre-school children were immunized by a drive initiated by Dr. Shirley Wynne to wipe out diphtheria by immunizing every child in the city. One-half million children were thereby immunized and the number of cases and deaths decreased by one-half in ten years and again by another half in the past two years. If the same organized enthusiasm can be maintained, diphtheria will be conquered and eliminated.

Scarlet fever is less common than measles, whooping cough and diphtheria, and has a lesser degree of transmissibility. Dochez, in 1919, was the first to demonstrate the particular streptococcus causing scarlet fever. He found that the toxin elaborated by this organism in the throat was absorbed and produced a rash and symptoms of the disease in a way comparable to the mechanism in diphtheria. A horse was immunized with the hemolytic streptococcus and the serum used by Blake, of Yale, was found curative of scarlet fever. The Dicks of Chicago, in 1923, perfected the toxin and tested the susceptibility of children to scarlet fever. Repeated injections of this toxin were found to have the power of producing an immunity to the disease. With the perfection and administration of the immunizing material, scarlet fever can be eradicated when early evidences of its occurrence in a community are observed.

Measles is the most highly infectious of the communicable diseases and but few children escape. Five hundred infants die each year from the complications of measles, particularly from pneu-
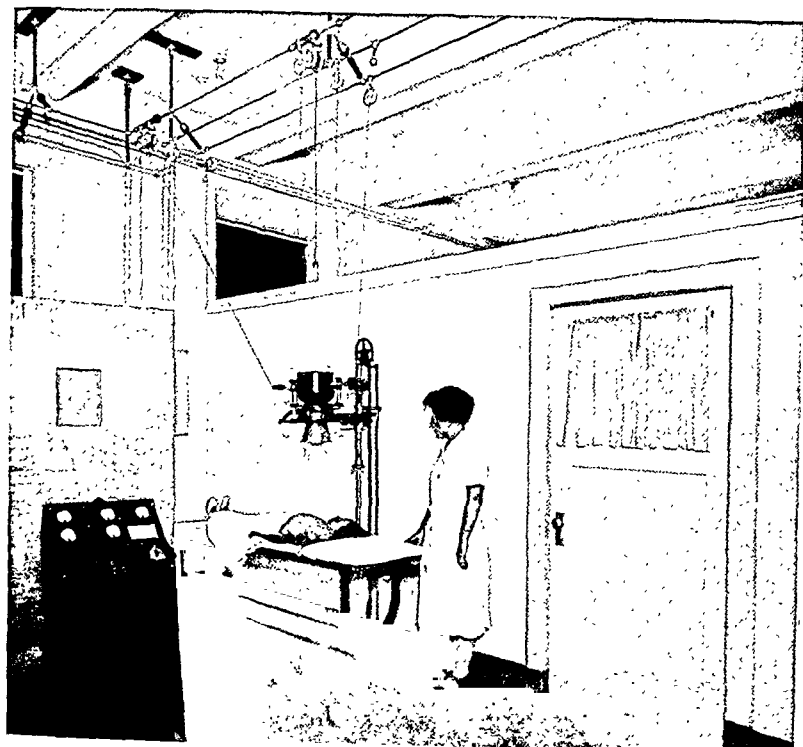
The Clinic for Nervous Children.

FIG. 6.

A Dental Unit of the Health Clinic.

monia. The causative organism of the disease is as yet unknown but it has been observed by Park that immunity which follows an attack of measles is due to a protective substance which remains in the body throughout life. This immune material is most abundant shortly after convalescence from measles. Five cubic centimeters of blood from a convalescent child when injected into an exposed infant will either prevent the development of measles or greatly lessen its severity if given within four days of its exposure. On the other hand, one ounce of a parent's blood who had measles in childhood is of almost equal value in the protection of the children of the family from acquiring this universal disease.

Two communicable diseases—infantile paralysis and mumps— have recently been found by Flexner and others to be due to a filterable virus. Both leave antibodies in the blood of convalescent children in the same degree as those having had the measles. We use, therefore, the serum of convalescence or a large amount from those who had the disease years ago as a preventive. Convalescent serum, thus given, prevents many of the complications of these diseases. Smallpox is the classical illustration of the value of preventive medicine of childhood. It was once a scourge of mankind and today is relatively unimportant. In California, since the repeal of the vaccination law, there has been an increase in the incidence of smallpox with thousands of deaths—all preventable.

Hydrophobia developing in those bitten by rabid dogs can be prevented by the Pasteur treatment. The stray dog should be kept alive and observed for several days for rabies. Microscopic examination of the dog showing signs of rabies will then reveal the disease and the child may be immunized accordingly. Typhoid fever is now a rarity in children but it does occur, particularly in summer camps. Children should be inoculated with the vaccine whenever they travel into regions of uncertain milk and water supply.

Tuberculosis in infants and children is derived from human contact or from infected milk. The danger from milk has been removed in large cities by pasteurization. The danger of human infection has been partly met by improving the health status of the child, so that in the presence of infection the disease will not be as progressive, and recently, by vaccinating the infant with an attenuated culture. Von Pirquet, in Vienna, devised the tuberculin reac-

tion to test the presence of the disease in children. It has been found in the last two decades that the entire race is infected with tuberculosis before the second year of life, producing what is known as the healed primary infect in the lung. Subsequent exposures to tuberculosis flare up this early process, with the resultant spread of disease to all parts of the body.

Calmette and Guerin, of the Pasteur Institute, have evolved in 1925 a vaccine prepared from an attenuated culture, the administration of which is destined to prevent the development of tuberculosis. It is either fed to the new-born infant or injected in a minute amount into older children. Ten thousand babies have thus far been treated with a marked decrease in the disease in comparison with control babies.

Syphilis is the chief cause of fetal death. The treatment of hereditary syphilis is its prevention. Transmission of the disease is practically nil if the luetic mother is treated before and during pregnancy. Bordet developed a method which Wassermann perfected for the diagnosis of syphilis by blood examination. Intensive study of prenatal blood will eliminate hereditary syphilis as a communicable social problem.

III

The greatest philosopher among the ancients on child feeding was Hippocrates, the famous priest of Aesculapius, officiating in the celebrated Health Temple of Cos in Greece in the days of Socrates and Plato. He and his successors for two thousand years accounted for the disappearance of food as "insensible perspiration" and "heat" without any real understanding of their meaning.

Sanctorius, in 1604, weighed himself before and after meals in order to determine the balance between food and the amounts of "insensible perspiration." Boyle, in 1627, demonstrated the dependence of man upon the air he breathes. Later, Lavoisier clinched the respiratory process of man in relation to his food intake. Leibig was the first to present clearly the difference between protein, fat and carbohydrate. Rubner, in 1892, established the fundamental law that energy is neither created nor destroyed. From these basic facts emerged the science of nutrition.

Artificial feeding first became prominent early in the fifteenth century. Cow's milk, goat's milk, bread-and-sugar displaced breast

feeding when necessary. The mortality of the breast-fed babies was about a third of hand-fed, and particularly so in the foundling hospitals. Innumerable treatises and poems on child health characterize that period of interest in the cause of child health. The food requirements of normal and sick children were first studied scientifically by Rubner and Hubner, in 1898. They demonstrated that metabolism during growth is a function of the surface area of the body. Hitherto, the progress of growth and development was evaluated in terms of weight alone, introduced by Allfeo, in 1878. Talbot, Benedict and others in this country have refined the experimental technic pertaining to the metabolism of childhood.

The first health centers to encourage breast feeding and advise in the artificial feeding of infants were started by Budda, in Paris, in 1892. These so-called milk stations were subsequently opened throughout the continent, and in this country by Strauss, in 1893.

Chemical studies of breast milk as the complete food sufficient for the growth of infants revealed the basis of effective infant feeding. Mendel and Osborn found that eighteen amino acids derived from proteins are required for growth. Hopkins, of Cambridge, demonstrated the vitamin requirement during growth. McCollum, of Johns Hopkins, discovered the presence of vitamin A in fatty foods and Bloch, of Copenhagen, found it indispensable for growth and the prevention of xerophthalmia. Funk, in 1912, discovered vitamin B in rice bran curative of a nervous disease—beriberi. Hess, in 1914, demonstrated that vitamin C contained in fresh fruit juices is curative of scurvy. Park, in 1920, demonstrated that vitamin D, present in cod-liver oil, was curative of rickets. Hess and Steinbock, in 1924, discovered that the irradiation of food with ultraviolet conferred upon it the antirachitic property of vitamin D. Evans, in 1923, discovered vitamin E as the antisterility factor in meat, whole grains and vegetables.

Nutritional advances have made possible the prevention of deficiency diseases widespread amongst infants and children. Rickets is a nutritional disease of civilization due to faulty mineral metabolism resulting in retarded deposition of calcium salts. It has gradually become universal in the course of the transition of human life from outdoor living to modern housing. The disease was first recognized clinically by Glisson, in 1628, as one of softening of the bones and the empirical treatment then was the administra-

tion of cod-liver oil. The last ten years have cleared up the essentials pertaining to the mechanism of bone formation. The bone substance consists of calcium phosphate and carbonate precipitated from the child's blood. The absorption and the rate of precipitation of these salts is dependent upon the presence of vitamin D as a catalyst. Vitamin D may be obtained in the body in a variety of ways—in fatty foods like cod-liver oil, egg yolk, butter; by exposure of the child's skin to ultra-violet, thus making vitamin D from the body fat; by the irradiation of certain foods by ultra-violet and then consuming them; or by maintaining the child outdoors exposed to sunshine, or indoors wherein glass has been substituted by ultra-violet permeable glass. It is a matter of economic choice which procedure is resorted to for the daily vitamin D intake.

Goiter occurs most during pubescence in regions remote from the sea. The incidence follows the iodine content of water. Marine, in 1917, demonstrated the possibility of controlling the development of goiter by the routine administration of iodine salts to older children. The iodine as a specific against goiter is combined in chocolate tablets or in table salt and offered universally in those regions where the food lacks natural iodine. In Switzerland and the Great Lakes water supply is iodinized twice a year to protect progeny from iodine deficiency.

A great source of community waste results from preventable sickness and death amongst mankind. The greatest losses occur at the beginning of life. In 1900, 17 per cent. of the babies counted then died that year, while in 1926 the infant mortality was only 7 per cent. The mortality of children from one to four years has declined from twenty-one per thousand to six per thousand. Between five and nine, the mortality has declined from five to two per thousand. Between ten and fourteen years, the mortality declined from three to two per thousand. But the mortality in each age group can be further reduced. The report of the children's bureau reveals 1 per cent. of school children mentally defective, 1 per cent. handicapped by potential heart disease, 5 per cent. with potential tuberculosis, 15 per cent. with diseased tonsils, 20 per cent. with defective teeth, 25 per cent. with defective vision, and 25 per cent. with malnutrition. And the present appropriation for school health work is sixty-five cents per child per year! The physical imperfections of childhood reflect on the stamina of adult population. Our first
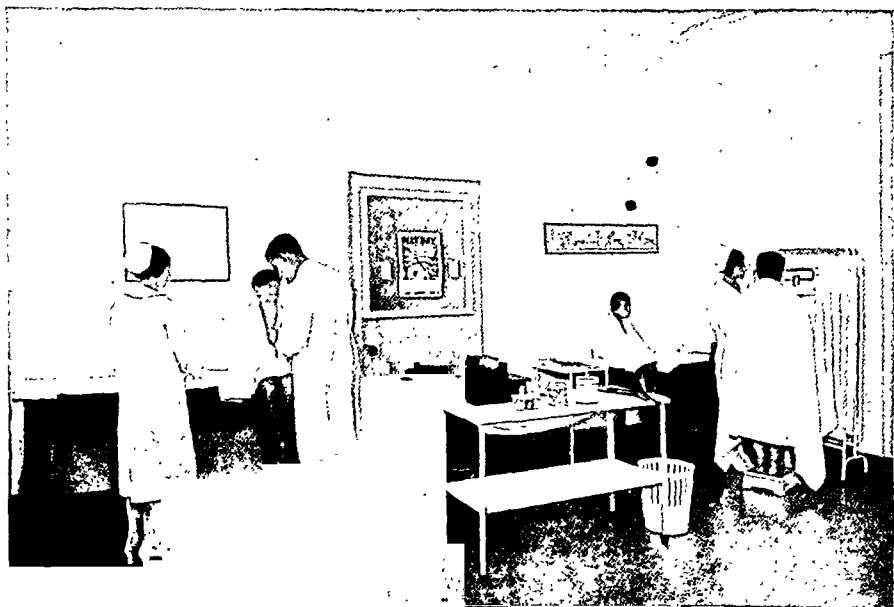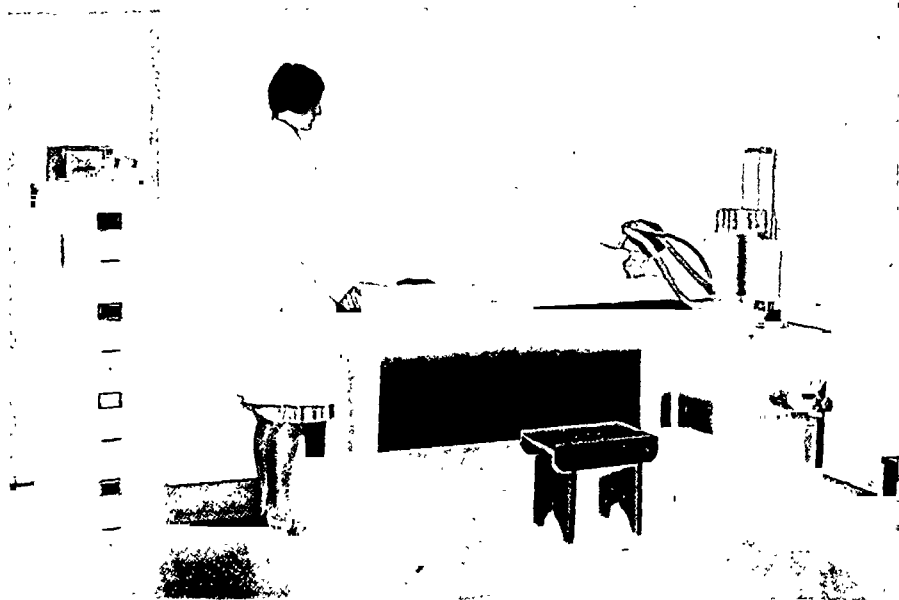
The Clinic for Obese Children.

national health inventory came through the World War, when five million young men were examined as to their physical fitness for military duty. And one-third were found unable to serve because of physical unfitness!

IV

The child as a whole was first studied in the middle of the last century by Tiedemann, in Germany, and Restif, in France. Darwin kept daily record of the development of children's activities. G. Stanley Hall refined the methods of observation. The behaviorists—Watson, Smith, Guthrie and others—developed harmless academic speculation. Freud evolved life about sex. Adler and Jung explain individuality on the basis of human weakness.

The first steps toward the organization of study in child development for the promotion and correlation of research relating to the growth of the child have been taken by the National Research Council, in 1923. The whole field of child health was then transferred from speculative child philosophy to substantial science. Child development thus became a protean kind of postnatal embryology, a focal field for psycho-biological medical knowledge. Growth is thereby conceived as a uniform concept which depolarizes undue deviations between mind and body, between heredity and environment, between health and disease. However, behavior always tends to fall in order of patterns. Even the random behavior is obedient and patterned, characteristic of species and of age. Behavior patterns are directly determined by the neural counterparts of the central nervous system and evidently by bio-chemical control. They yield to quantitative study and furnish the orientational norms which are necessary for the measurement and the early diagnosis of developmental defects and deviations.

The child-health movement as a phase of public health is of recent origin. It received its impetus during the World War, when, in the course of routine physical examinations, physical deviations and defectiveness were rampant amongst the youth of the nations. It has attracted the attention of social workers, of non-medical health workers and, without adequate guidance or participation, of medical men and women, and as a result deviated into fields of activity that are strictly far from the purposes of child health. The lack of interest on the part of the physician and the variegated child hygiene

activities is partly due to the propaganda nature of this work without including the knowledge and experience of the medical profession upon whom finally rests the alleviation of the early disturbances that prevail in childhood.

The first development of child hygiene in this country began in 1905 in the school system when physicians were added to its staff in an effort to prevent the spread and development of contagious diseases. The subsequent decrease of contagion led to another phase of preventive medicine in the cause of infancy. The high rate of infant mortality during the summer which resulted from diarrheal diseases was first studied in 1907 by the American Association for the Prevention of Infant Mortality. They found that it was impossible to lower the rate of infant mortality by the adequate treatment of sick infants but that proper supervision of the infant throughout the year would contribute greatly to the prevention of these summer diseases. This led to the development of the home nursing service and special summer clinics for the early recognition and care of summer diseases. But the great emphasis was placed more on pure milk and refined milk mixtures and thus deviated the real purpose of the preventive work into clean milk stations. They were valuable for awakening community interest in clean milk supply and appropriate laws guaranteeing clean milk. But, nevertheless, the milk *per se* was detrimental to infant welfare. They emphasized artificial feeding rather than maternal nursing. They carried on for several years before realizing that the chief purpose of the infant welfare work was educational rather than relief by prescription and so there was a steady transition from the milk stations into centers for the education of mother and the supervision of well babies.

The methods of child hygiene, developed from the public-health standpoint, are not ideal for the application of preventive paediatrics. They are concerned with the care of the well child and leave the same child ill in the hands of another physician. It is unsound fundamentally. Health and ill health in a child are but different states of an interfering process proceeding from the same organism. The prognosis of a sick child depends very largely upon its previous constitutionality.

Predestination of certain disease entities applies to all phenotypes at birth. They are born into an environment with definite tendencies to specific disease—pulmonary, gastro-intestinal, nervous,

and so on. These early manifestations may be recognized medically by continuous supervision of the child from birth. They constitute the basis of preventive paediatrics in relation to the individual child. No general health slogan can ever apply to such a child. They represent the group for whom the greatest good can be accomplished by the modern methods of prevention. It is the early recognition of the types of disease that such children are heir to that makes for the best management of the illness complicating the growth of such children. The responsibility of the health of the child divided between the home physician and the health physician is detrimental to the interest of the child.

The hospital has outgrown its usefulness for the prevention of disease in infancy and childhood. Its organization is devoted to the diagnosis and treatment of sick children. And once that important service has been rendered in the alleviation of the symptoms of disease, the hospital ceases to function for the subsequent welfare of the child. The hospital discharges the convalescing child so long as its physiologic functions proceed normally. It is concerned only with reëstablishment of necessary vital processes of the child's life.

But the child is more than an ensemble of tonsils, teeth, lungs, heart, liver, intestines, spine, hands and feet. The child is a dynamic personality in the making. It is a composite individuality with evanescent manifestations of growth and development. It is a veritable little laboratory transforming food into growth, experience into life habits, environment into personality. And depending upon the character of the intake does its composite body develop at a maximum or minimum.

The newer medical approach is to supervise normal growth and development. The child is examined with a view towards optimum function of all its organs individually and the child as a whole. The eyes are studied for maximum range of vision rather than for conjunctivitis; the ears for acuteness of hearing rather than for abscesses; the nose for adequate breathing rather than for foul discharges; the mouth for functional alignment rather than for fetor; the brain for mental growth rather than for meningitis, with a view toward accelerating the level of his life's heritage rather than from the standpoint of labeling him as the bearer of one disease or another.

The guiding motive in all child-health movements today is reduc-

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The guiding motive in all child-health movements today is reduc-

tion rather than medical relief. It involves all periods of growth and development from the moment of conception through adolescence—prenatal clinics, new-born clinics, infant welfare stations, preschool clinics and child-health clinics. Various organizations that began with a particular phase of child life have merged into the American Child Health Association, in 1923. State organizations pertaining to child health have all been organized into a federal children's bureau, in 1912. The purpose of these organized bodies is to educate the parents in the methods necessary pertaining to normal growth and to the development and the education of the child in correct life habits.

The universal urge of preserving childhood makes great the demand for continued supervision by a trained observer, the physician trained in preventive paediatrics. Health literature, health lectures are necessarily general in scope and rarely apply to the individual needs of the child. Baby shows, health contests, weighing festivals are superficial propaganda to arouse interest in child hygiene. Superficial examination of children is without value in the prevention of defectiveness in childhood. Unless a well-defined program includes trained medical observers to detect early manifestations of disease, potential defectiveness or mental psychological deviations from the norm, the individual child receives no benefit from the multiplicity of propaganda. Furthermore, accurate knowledge of the health status of the child alone does not satisfy the crux of the growth situation. The health program must necessarily include measures for the correction of the defects detected early.

The physician must use every resource to protect the child from his environment, while the health officer must strain to protect the environment from the child. It is the same telescope but they are looking through it from different ends. But the world is full of such differences in points of view—the lawyer and the judge; the mortician and the clinician; the bootlegger and the prohibitionist. If each were to address each other, antithesis might result in synthesis. Health wisdom has permeated the masses. Formerly, the public idea was that doctors are omniscient about disease so that it was safer for the laity to be ignorant of things beyond them. Now the individual is provided with arms and armor so that he may cease to be a helpless parasite and play an active part in his own defense by warding off the arrows of death for himself.

CHILD HEALTH EXAMINATIONS

By MORRIS STARK, M.D.

Attending Pediatrician, the Heckscher Institute for Child Health

IT HAS been of special interest to me to have the opportunity of examining a group of children just below and within the school age who have been brought for medical examination not because their parents thought they were ill, but because they were required to undergo a physical examination so that they might join a class of other children taking special activities. In other words, they were children who were assumed, by their parents, to be in ordinary good health.

Before going further into this discussion, let us understand the viewpoint and standards assumed in the examination of these children. Let us not confuse the absolutely normal child with the merely healthy child. The absolutely normal child includes the healthy child, while the healthy child does not, by any means, imply the absolutely normal child. We are here concerned with finding out, if possible, by a careful physical and clinical examination, whether the child before us is at·the present examination infected by disease, or is hampered or has been seriously injured by the results of previous disease or accident or developmental defect, and if he can be helped or cured by either definite therapeutic measures or intelligent advice.

Most of the children brought for examination were considered by their parents to be in perfect health, and a great many of them really were, as far as could be ascertained at the time. Unfortunately, a great many of them were decidedly not in good health and it is with these that we shall concern ourselves at this time.

First and foremost, I was impressed by the great number of heart lesions and heart abnormalities that were found, and, added to this, the degree of undernourishment and underdevelopment that could be directly and indirectly traced to these conditions. From slight mitral rubs that could be detected only by careful auscultation ranging to bruits and apex impulses that could be felt with the hand or readily seen. All types of irregularities, from an occasional extra

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systole up to the perpetual irregularity of the heart-beats, some loud and sharp, others weak and muffled, suggesting an auricular fibrillation that would hardly require an electrocardiogram to verify, were present. In several cases the decompensation found after slight exertion seemed far from safe. These conditions, though very evident, were either not noticed at all by the parent or were considered of not sufficient importance about which to consult medical advice. I recall one case where there was a marked systolic retraction of the thoracic wall in a rather tall, lanky girl whose mother recalled a very definite history of a prolonged illness with "lots of growing-pains" nine years previous, but she had been perfectly well since, without even the pains in the chest which I tried hard to get both the girl and her mother to admit. The heart-beat was markedly irregular, and there was a distinct rub that could be heard now and then without reference to any valve or period of the cardiac cycle. The cardiac dulness was only slightly enlarged. This was probably one of those adhesive pericarditi that Lengsfeld says is more frequent in children than is usually diagnosed. The mother of this child thought nothing was wrong and wanted the girl to join a swimming and dancing group. In many of the cardiacs we find great difficulty in getting the previous history and only after persistent and careful questioning can we jog the possibly convenient memories of the parents sufficiently to recall a birth history or sore or growing-pains or undiagnosed fever or dyspnea on slight on or other related history to help us in getting at the etiology. were they reluctant but even resentful when closely questioned. Diseased tonsils, purulent retropharyngeal or anterior nasal discharges with possibly infected accessory sinuses were excluded wherever possible or, if present, the cases were referred for further special diagnostic investigation and treatment.

Another series of rather interesting findings were those who had mild degrees of scoliosis, some so slight that it was barely noticeable, and yet it is these very slight cases that are of special interest in this connection. Careful measurements were taken of the comparative length and circumferences of both lower extremities. Special attention was given to the comparative tonicity of muscles and activity of reflexes on the two sides and in some of these cases we felt sure that we had the results of unrecognized previous poliomyelitis. We then

went into the previous history in minutest detail as to unrecognized
fever (perhaps with slight pain in the neck muscles), coarse tremor
(nervous shaking different from anything the child ever had before
—not a chill), perhaps soreness in back for a day or so when the
child bent forward, difficulty in swallowing without real pain (food
stopped for a moment on the way down) or (water got into the back
of the nose when swallowed). When the child got out of bed did
it seem to stumble a little, or trip easily, or get tired one leg sooner
than in the other when walking, etc. ? We were able in four cases
to get a most presumptive history of an abortive poliomyelitis. Of
course, it would be interesting if it were possible to get the blood
serum of these cases and test their immunizing power in animal
experiments. If we were satisfied that some of these cases required
postural treatments we could give a more definite prognosis as to
the ultimate result of treatments as compared with the usual postural
cases due to improper muscle training or other simple causes.

Still another group of interesting cases that one sees in the exami-
nation of so-called "not-sick" children consists of undersized, overfat
children (not cretins, chondroplasiacs, dwarfs, etc.), or else those
showing gradual loss of weight without loss of appetite or other out-
wardly apparent cause in whom glycosuria was never demonstrated,
temporary or otherwise. These should always have a blood-sugar
done, if possible, as part of the routine examination. It is surpris-
ing how many of these children show a hyperglycemia without
spilling into the urine. Intelligent treatment of these cases fre-
quently causes the disappearance of symptoms that seemed due to
undiscoverable causes, especially since one is so frequently satisfied
with a urine examination alone. Priesel and Wagner, of Vienna,
believe that diabetes mellitus in children is dependent upon a con-
genital minus variation of the islands of Langerhans so that a latent
diabetes is dependent upon the number of available pancreatic
islands somewhat in the nature of a malformation. If to this one
adds the high sugar tolerance of some kidneys before "spilling"
occurs, one may well find justification in doing a blood-sugar in some
of the types of cases referred to.

The question of general nutrition is also of great importance
in the routine health examination of the child, not only as to whether
it is fat or thin, but as to how fat or how thin? Muscle tone, color,

systole up to the perpetual irregularity of the heart-beats, some loud and sharp, others weak and muffled, suggesting an auricular fibrillation that would hardly require an electrocardiogram to verify, were present. In several cases the decompensation found after slight exertion seemed far from safe. These conditions, though very evident, were either not noticed at all by the parent or were considered of not sufficient importance about which to consult medical advice. I recall one case where there was a marked systolic retraction of the thoracic wall in a rather tall, lanky girl whose mother recalled a very definite history of a prolonged illness with "lots of growing-pains" nine years previous, but she had been perfectly well since, without even the pains in the chest which I tried hard to get both the girl and her mother to admit. The heart-beat was markedly irregular, and there was a distinct rub that could be heard now and then without reference to any valve or period of the cardiac cycle. The cardiac dulness was only slightly enlarged. This was probably one of those adhesive pericarditi that Lengsfeld says is more frequent in children than is usually diagnosed. The mother of this child thought nothing was wrong and wanted the girl to join a ... ing and dancing group. In many of the cardiacs we find great difficulty in getting the previous history and only after persistent and careful questioning can we jog the possibly convenient memories of the parents sufficiently to recall a birth history or sore throat or growing-pains or undiagnosed fever or dyspnea on slight tion or other related history to help us in getting at the etiology. only were they reluctant but even resentful when closely questioned. Diseased tonsils, purulent retropharyngeal or anterior nasal discharges with possibly infected accessory sinuses were excluded wherever possible or, if present, the cases were referred for further special diagnostic investigation and treatment.

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went into the previous history in minutest detail as to unrecognized fever (perhaps with slight pain in the neck muscles), coarse tremor (nervous shaking different from anything the child ever had before —not a chill), perhaps soreness in back for a day or so when the child bent forward, difficulty in swallowing without real pain (food stopped for a moment on the way down) or (water got into the back of the nose when swallowed). When the child got out of bed did it seem to stumble a little, or trip easily, or get tired one leg sooner than in the other when walking, *etc.*? We were able in four cases to get a most presumptive history of an abortive poliomyelitis. Of course, it would be interesting if it were possible to get the blood serum of these cases and test their immunizing power in animal experiments. If we were satisfied that some of these cases required postural treatments we could give a more definite prognosis as to the ultimate result of treatments as compared with the usual postural cases due to improper muscle training or other simple causes.

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activity, general mien—all enter into the case. I do not include the undernourishment due to recent or present disease, poor health, poverty and privation, nor to dietetic ignorance or indulgence. We must go into the subject of heredity, environment, race, habits, and dietetics before we can decide upon the form for the case before us. Having arrived at that we are in a position to decide just what measures are to be adopted to bring that individual as near as possible to his personal or class norm. It is presupposed, naturally, that we have eliminated every possible deterrent in the result of our physical and clinical examination.

We must not omit from our consideration the occasional endocrine dyscrasia that we are forced to face, which, in themselves, are not the causes of definite disease but which, nevertheless, alter the picture and in most cases indicate therapeutic measures without which others would fail. The hyperthyroid, the mild hypothyroid, the hypogonad, the Froelich, the sub-mental—all must be taken into consideration, and most of these become behavior problems independent of what might be accomplished by gland therapy. The severe cases of cretinism, mongolism, morons, idiocy and the like are never brought to child-health classes.

Cases with serious skin disease are also seldom brought to these classes, due, undoubtedly, to the fact that parents know them to be manifestations of disease and they further know that their children would not be acceptable to other parents whose children attend special classes in an institution. Pediculosis and mild eczemas are occasionally encountered. The former is usually not recognized and the latter not of sufficient importance to exclude the child.

In discussing the tubercular infections which are not believed to exist or at least are not willingly admitted or believed in by the parents, we constitute a problem that is of primary importance in making these health examinations. The handsome, fairly nourished child or else the undernourished pale child or the one with the unusually red cheeks (sharply outlined circles) with the piercing dark eyes, long black drooping lashes, heavy eyebrows, velvety skin with its excess of hair (especially in the presence of cervical adenopathy) is always taken as a suspicious case and all available diagnostic means and aids are used to eliminate every possibility of an

active process going on.   Careful exhaustive history back into in-
fancy and possibility of contact are considered.

Postural correction, personal hygiene, dental care and hygiene,
orthodonture—all are important factors in improving or maintain-
ing the health of the child.

This work is carried on with the efficient aid of the laboratory,
and a staff of consulting specialists gives work of this kind the
security and thoroughness which it demands.

In conclusion, I wish to make the plea that more frequent health
examinations of children be made, not only when their parents be-
lieve them to be ill, but also when from previous knowledge of earlier
conditions one suspects or fears the possibility or probability of
serious sequellae.   The timely recognition and treatment of these
might spare the patient serious discomfort or disability in later life.

COMPARATIVE STUDY OF POSTURE IN FIRST AND SECOND DECADE OF LIFE

BY KRISTIAN G. HANSSON, M.D.

(Preliminary Report from the Department of Posture, The Heckscher Institute
Child Health, New York City)

ALL through the ages the external appearance and its relation to the internal mechanism has been a subject of interest and investigation. The animals and the plants have been judged by their looks. The result is that we know more about an animal's or plant's function from analyzing their exterior than we do about our own body. It is only during the last twenty years that medical men have directed their investigations toward body mechanics. We owe most of our present knowledge to Dr. Goldthwaite, who began analyzing the effect of postural abnormalities on the body and also the most favorable positions of the body.

It soon became evident that some kind of postural standards was necessary. Drs. Lee and Brown of Harvard undertook to examine 700 freshmen and this study with the work of Dr. Armin Klein form the basis for our present posture standards, which can be obtained from the Children's Bureau, Department of Labor, Washington, D. C.

If, however, these standards are applied to the children of the first decade of life and especially to the pre-school child, we run into errors, which are misleading to the doctors, and add unnecessary treatment to the child and worry to the parent. Using these adult standards in my own practice when I followed 300 children in a private school over a period of years I found postural defects as high as 85 per cent. in children under ten years of age.

These same standards used on pre-school children produce even more disappointing results. The following is a report that was submitted to me this winter from an organization in New York City interested in the health of pre-school children. According to this report, which analyzed 815 children between the ages of two and six, the summary was as follows: (1) 50 per cent. had round backs, 30 per cent. had hollow backs; (2) prominent abdomen was a

feature in 95 per cent.; (3) Harrison's groove occurred in 70 per cent.; (4) 90 per cent. had pronated feet, flat feet occurred in 85 per cent. It occurred in 98 per cent. of the two-year-old children and less frequently with each advancing year.

Directing our thoughts to the changes that take place from the embryo into the full-grown human body we observe many interesting facts. The embryo is laid down as a quadruped. The spine shows only one long curve with the convexity backwards, the shoulder blades are high up on the spine and the angle between the spine and the femur is less than 90°. The comparative length and attitude

FIG. 1.

2 mo. (fœtal)   5 mo.   Newborn   2 yrs.   6 yrs.   Adult
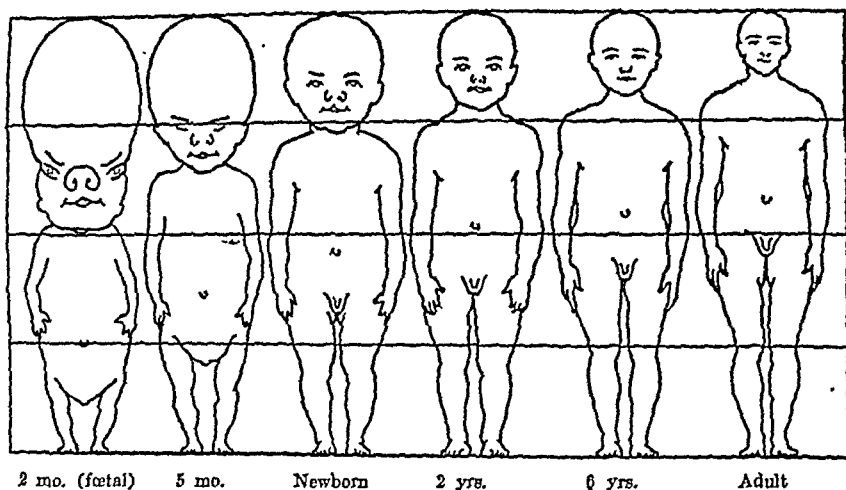
of the extremities suggest creeping on all fours rather than the erect posture. The relation between chest and abdomen in the embryo suggests the retreating chest and protruding adipose abdomen of later life. Looking at the posture standards above we see a number of curves developed in the spine and the extremities are parallel with or in the same general direction as the spine. The thoracic cavity has a circumference greater than the abdomen, which latter is restricted.

The relative changes in the body are well shown by the above pictures of the developmental growth from an embryo of two months to an adult. (Fig. 1.) The trunk retains about the same relative size (about 45 per cent.). The upper extremities reach about 10

per cent. of the body at birth and maintain the same relative length. The lower extremities, however, reach 20 per cent. at birth and 35 per cent. at adult life.

The muscular system is about 25 per cent. of the body at birth and 40–45 per cent. in adult life. The visceral system is largest in embryo, about 35 per cent., at birth 21–24 per cent. and in the adult 10 per cent. of the body.

Among the organs, the liver is decreasing from 10 per cent. in the third prenatal month to 5 per cent. at birth and in adult life to 2.7 per cent. of the body. The gastro-intestinal tract, the kidneys and spleen reach their maximum relative size at birth. The first decade of life lying between the embryonic quadruped state and the fully developed biped posture of the second decade, should therefore naturally show the gradual change from the former one into the latter one.

This transitional stage of the first decade is a very sensitive formative period of life, both as to physical and mental development, and we must be careful before we stamp a child below ten with postural defects. It is evident that any posture standards will depict only the average and that great variations are found within the normal. These variations are germinal and somatic. The former are hereditary transmissions of differences in the germ plasm producing different individuals. The somatic variations are due to environmental influences such as nutrition, climate, disease and training. While we do not expect to correct the germinal variations we are able to influence the somatic defects.

At the Preventive Paediatric Clinic of the Heckscher Foundation we are now endeavoring to work out some posture standards that can be used for children of the first decade of life. These standards will be based on a study of 5,000 children of this transitional period of life.

TREATMENT OF WEAK FEET IN CHILDREN

By H. E. READING, M. D.

Associate Orthopaedist, the Heckscher Institute for Child Health, New York City

THE term "weak feet" has been synonymously referred to in the past as "flat feet," "pes planus," "pronated feet," and so on. This condition is very prevalent in both children and adults, being commonly met with in children who are brought to the average orthopaedic clinic. Within the last few years practitioners, school nurses and even mothers have become quite alert to recognize the potential possibilities in a child's foot showing deviations from the normal, if permitted to go untreated until adolescence. As a rule, symptoms of pain and disability are not manifest until some years have elapsed following puberty.

The etiology of weak feet has been written of by various men, but, as yet, no definitely proven cause has been determined. It is quite possible that this condition is analogous, at least in etiology, to that of congenital dislocation of the hips, or club feet—the latter two, of course, being of severe degree as compared to the subject under discussion.

The anatomical and functional considerations underlying weak feet are many in number, only a few of which will be discussed in this brief paper. Laxity of ligaments and tendons about the ankle-joint are from a mechanical standpoint an important factor in permitting weakness or instability of the foot and ankle for purposes of bearing body weight or walking. Weak musculature of the leg is indirectly responsible in producing a "weak ankle." This condition is frequently seen in undernourished children, and especially following the exanthemata with resulting prostration and marked loss of muscle tone in general. A very mild case, which would otherwise go unnoticed, may in time present definite evidence of weak feet as a result of improperly fitting shoes. Malformations of the tarsal bones and deformities following the different forms of paralysis are clinical entities quite different from that of weak feet.

Children, and especially so as adolescence is reached, can be

classified as possessing one of three types of feet—the high-arch, the medium-arch or the low-arch type. Among the eastern races and especially the negro the low-arch type predominates. Treatment of the feet should never aim at a change from the low arch to the high arch or *vice versa*. It has been commonly noticed that a child's foot will simulate that of its parents even to the extent of inherited deformities.

Diagnosis.—The younger the child the more tender are the body structures so that passive movements are quite free. The potential weak foot in a baby reveals sufficient laxity of the ligaments about the ankle to permit the examiner to passively dorsi-flex or outwardly rotate the foot to a marked degree. When such a child commences to walk he is noticed to bear the body weight on the inner sides of his feet. This observation becomes more pronounced as the child grows older. Frequently a mother will call attention to the fact that her child, after two years of age, shows uneven wearing in the soles of the shoes—this being in some cases early evidence to warrant the advice of a physician. Until the period of adolescence, pain or fatigue following walking or exercises is seldom complained of by the patient unless the condition is complicated by a localized infection or arthritic changes about the foot.

Treatment.—Treatment of weak feet will be discussed according to age periods.

In the baby, treatment should be instituted as early as the sixth month of life. If, in the opinion of the practitioner, the condition seems to be severe, the best practical course to follow is to apply a fixed dressing to maintain the foot in marked varus and at a right angle with the leg. In our practice we prefer to use a plaster-of-paris dressing, previously applying a layer of sheet wadding, especially padding the heel and the malleoli. The plaster should extend from the end of the toes to just below the knee. The use of fixed dressings has proven to be efficient, and produced desirable results in the shortest space of time as compared to other methods at our command. The plaster dressing should be changed every ten days, for a period of one month. Before re-applying the dressings, the foot should be washed with warm soapsuds, thoroughly dried and talcum dusted over the skin of the foot. When the dressings are discontinued the patient should be fitted with a light-weight, alumi-

num, double, upright brace reaching to the knee, and having a foot plate bent at an angle so as to support the foot in a position of varus. The metal splint should be removed to permit massage of the legs, ankles and feet several times a day. As soon as the child is ready to walk the shoes should have an elevation of one-sixth to one-quarter inch on the inner borders of the soles.

After the fifth year of life fixed dressings to maintain the foot in an over-corrected position are unnecessary unless the condition of weak feet is of severe degree. As a rule, foot exercises and a corrective shoe are sufficient to bring about the desired results.

Unless it be a precocious child, coöperation is difficult in carrying out active exercises in a child under the age of five. For the sake of simplicity only two sets of exercises will be mentioned which have in the past given good results, and are easily carried out by the patient. The first group comprises three different steps, as follows: In the first position the child stands erect, the great toes touch one another and the heels are spread apart as far as possible. Secondly, the subject in this position stands on the sides of the feet, the toes being flexed downward toward the floor. Lastly, maintaining this attitude, the patient is to walk without changing the position of the feet. In the second group the child is taught to pick up such objects as a lead pencil or a very small inflated rubber ball with the toes.

In the first group relaxation of the tibialis posticus muscle and tendon, and also the structures in relation to the long plantar fascia are aimed at. In the second group, hyper-flexion of the toes is carried out, the small muscles of the toes are exercised and the anterior arch is permitted to relax.

SHOES FOR THE GROWING CHILD

When first permitted to walk, the baby's shoe should be of very soft material, little attention being paid to other details except for an appreciable snug fit about the heel and plenty of toe room. In the average case of weak feet in children between the ages of two and five, a shoe having plenty of room for the toes and a snug fit about the tarsal joints and heel will be beneficial. A wedge of one-sixth to one-quarter inch on the inner borders of the soles and heels should be added.

In cases of weak feet of marked degree beyond four years of age, the shoe should have in addition to the latter specifications a light, flexible steel shank to extend from the heel to a point just behind the metatarsal heads. If deemed necessary in a given case, this shank could be so bent as to give support to the high-arch type of foot. The writer does not find it necessary to use steel arch supports in children.

It is surprising to note what a large percentage of cases of weak feet in children respond readily and rapidly when prescribed proper shoes and exercises, and only in the very young or very extreme cases are plaster-of-paris fixed dressings necessary.

PROCEDURES IN THE PREVENTION AND CORRECTION OF ORAL MAL-MANIFESTATIONS IN CHILDREN

. By RALPH HOWARD BRODSKY, D.M.D.

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THE oral cavity, by virtue of its anatomical position, occupies a very strategic and important status in the processes of living which culminate in the generic term, Life. It is universally understood that this part of the body is the portal of entry into the thoracic and gastro-intestinal tracts, but there are few who intrinsically understand and appreciate the bearing that the mouth and its associated structures has upon the entire head and its contents, especially in children.

I shall in this paper discuss only some of the important procedures pertinent to this subject. Odontologists recognize that there are many factors conducive to oral mal-manifestations, the most important of which may be enumerated as follows:

Dietetics
Systemic diseases
Habits
Orthodontic conditions
Retained and impacted teeth
Abnormal fraena labiorum
Cysts and tumefactions, etc.

First, let us consider dietetics, prenatal and postnatal. From the prenatal standpoint the pregnant woman whose diet is substantially deficient in the essential elements, not only subjects herself to oral vicissitudes, but also brings into the world a child whose tooth buds and osseous structures are, at the very beginning, malformed. This child may be seriously handicapped from the incipiency of his life. Postnatally, it is possible to assist him to a degree, dietetically, by virtue of the fact that the bone is quite plasic and considerably amenable to repair. The teeth, however, once formed, may be rela-

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tively influenced and manifest a tendency to become calcified or decalcified; but such conditions, nevertheless, as malformations, or hypoplastic formations in the enamel can in no way be repaired other than through the medium of external mechanical measures such as operative dental and prosthetic restorations. The child too, may develop a diathesis for caries, and unless this is checked at an early age there will be manifestations in both the deciduous and permanent dentition.*

A well-balanced hospital diet, rich in vitamins "C" and "D" should be utilized. Not only is it essential to offer the correct food to the child, but it is also necessary to insist that the required elements are consumed. Not infrequently, upon investigation, it is observed that the mother adheres strictly to correct dietary procedures in the preparation of foods, but that the child eats only those foods delectable to him and permits the essential substances to remain untouched.

The exanthemata of childhood often leave devastating results in the mouth. Unfortunately, during any high febrile condition, calcification of the developing teeth, either deciduous or permanent, is very markedly arrested, although the tooth continues to grow. Later when the tooth erupts it is observed that there are deep pits ~ 1 .ities in the enamel which correspond exactly in date to the of the febrile disease manifestations. Obviously, the correct .. . . for these conditions rests with the pediatrician in the pre- ν ι ·̈ ɔn of the diseases.

Habit formations often play an important rôle in mal-manifestations of the mouth in that they may be the etiology of many derangements. Thumb-sucking and similar auto-erotic conditions and habits effect marked anatomical deviations from the normal in the growth and development of the teeth and the jaws. Pillowing, lip, cheek, or finger biting and many analogous activities if repeated with sufficient frequency during early childhood leave distinct evidences though maladjustment of the occlusion or articulation as well as manifesting a resultant facial change.

It should be our aim to develop a dentigerous apparatus which

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* The writer is at present engaged in an extensive research in the subject of dietetics :: related to dental caries but is not as yet prepared to report on the finding.

FIG. 1.   FIG. 2.   FIG. 3.   FIG. 4.

FIG. 1. Infected superior left lateral, with relatively large cyst formation, prior to treatment.
FIG. 2. Root canal just filled prior to apicoectomy and removal of cyst.
FIG. 3. Same case one year later illustrating the beautiful and rapid regeneration which takes place in the mouths of the children. (Root filling appears to be incomplete, deceptively, due to removal of the apex of tooth at an oblique angle.)
FIG. 4. Case of cervical lymph-node involvement treated at a hospital dermatological clinic for several months with no success. After radiographic detection and removal of the infected retained root, the neck condition showed an immediate response. (The root was completely covered by mucous membrane.)
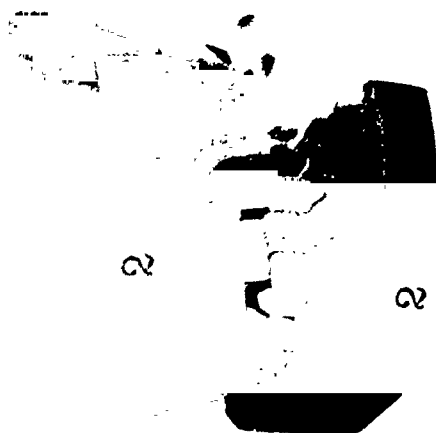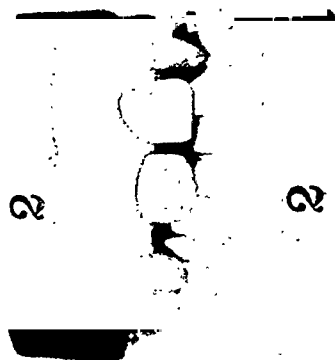
Fig. 4. Fig. 5. Fig. 6.

Fig. 4a. Models of a crossed bite condition. If not corrected this condition may be the etiology of a series of later oral mal-manifestations. Note the gingivitis already developing in the lower jaw.
Fig. 5. Models of the same case one week after treatment. Observe the facet formations on the tooth due to seclunical trauma.
Fig. 6. Illustrating the method of correcting the conditions by means of a tongue depressor exercise.

will approach the normal or perfect occlusion as nearly as possible. As soon as we deviate from this normal we begin to effectuate relative changes in the entire head. The mandible and maxillae through their articulation and contact with other bones of the head evince a definite relationship to these bones. Hence, if we permit, for example, a marked contraction of the arch of the superior maxillae during the developmental period of an individual, we produce a marked constriction of the paranasal sinuses. But this is not all. The entire musculature of the head necessarily becomes involved and through this loss of muscular equilibrium, the forces exerted by the muscles on the various head bones become so manifest that in the advanced cases we observe the very much narrowed and elongated head formations. It is logical to assume that where we have these marked constricting bony head changes we should also find intracranial changes, perhaps even to the degree that a mental abberation may result therefrom. It is therefore most important to preclude, wherever possible, conditions which will result in the constriction of the dental arches.

Among the factors which may be responsible for these marked contractures may be included premature loss of the deciduous, or loss of the permanent teeth with no provision made for their space retention. Resultantly, the remaining adjacent teeth begin a migratory process in an attempt to close the space. Not only do the jaws thus become maldeveloped, but by virtue of the constricting influence, there is usually not sufficient space for the eruption of the remaining unerupted teeth. This results in the impaction of these teeth, and we recognize that impactions may be the etiology of various types of neurological manifestations.

Realizing the importance of retaining the deciduous teeth until the normal time for their exfoliation, and being cognizant of the necessity of the maintenance of the permanent dentition particularly during the period of the development of the bones of the head, the writer has devised a simplified system of adequately retaining these teeth when their pulps become involved. In short, the method consists of utilizing in the root canal silver which is obtained by a reduction or precipitation process from an ammoniated solution of silver nitrate, the precipitant being eugenol. This is followed by filling the canal with a thin plastic mix of zinc oxide, eugenol, and

silver nitrate. Wherever possible this is supplemented by a simple periapical currettage or actual apicoectomy, with the aid, of course, routinely, of employing radiographs. In children this is relatively simple. The bone is quite plastic and repair is usually rapid. This technic may be employed in all children with the exception, however, of those who manifest systemic diseases and in whom we wish to eliminate every possible contributing etiological factor. In these children their susceptibility index is such that the presence of devitalized or pulpless teeth may act as a deterring influence.

Where we have of necessity resorted to the premature removal of teeth, simple orthodontia space retainers may be advantageously applied. It is likewise possible, through the employment of simple mechanical devices or muscle exercises, to prevent, or if already existent, to correct various types of orthodontic manifestations. It is first necessary to recognize and if possible to eliminate the causative factors which may include, in addition to the various habit formations, deviated nasal septa, enlarged terbinates, bony spurs, adenoids, or hypertrophied tonsils. In cross-bite conditions, conditions which are observed quite frequently, we may effectuate a cure by means of some simple device, such as a wooden tongue depressor to be utilized as an inclined plane. Auspicious results in the younger children are often manifested in one or two weeks after the assiduous use of the appliance.

Abnormal fraena labiorum are found often to be the cause of unusual spacing between the central incisors, resultantly displacing the adjacent teeth. The correction of this condition in a child is very easily effectuated. The procedure consists of removing, either by means of a small electro-cautery or a scalpel, a V-shaped section of the fraenum between the teeth and extending it to and including the perisoteum. This eliminates the bundles of dense fibrinous elastic tissue which act as a wedge between the teeth. The separated teeth are now ligated with a grass-line ligature, brought into lateral contact, and held there until the next adjacent permanent teeth erupt to act as natural retainers. Simple supernumerary teeth in the midline of either maxillae or mandible may be removed and the adjacent teeth ligated in the same manner.

It has been the writer's experience upon a number of occasions to observe children manifesting cervical gland involvements with

no visible oral sepsis, being sent from dentist to dermatologist or pediatrician with no apparent elimination of the condition. In these cases, through the medium of careful radiography, one often finds retained and infected root fragments which may have become completely covered by the mucosa overlying the alveolus and hence not recognizable clinically. Deep-seated caries causing a chronic infection of the pulp, and sometimes situated under extensive fillings may likewise give rise to involvement of the cervical nodes.

A condition relatively common and resulting often in febrile manifestations and which may terminate in convulsions is the laboriously erupting tooth in the infant or young child. The etiology is usually a thick, tense, fibrinous, and elastic membrane overlying the tooth and thus preventing its eruption. Simple scarification of this membrane brings no relief and may accentuate the condition. It is essential to make a' large and sufficiently deep incision in the membrane to actually free the tooth. In many instances this procedure will bring about an almost instantaneous relief.

In conclusion permit me to state that the mouth is often neglected by pediatricians. It plays an important rôle in the development of the head and in its association with general systemic conditions. Would that it were possible for the average, or sometimes even the superior pediatrician to make an intelligent oral diagnosis.

The beautiful old Latin aphorism, *Mens sana in sano corpore*, should be given greater cognizance, thereby rendering the human being more susceptible to Health, Peace, and Truth.

Further Contributions from the Fifth Avenue Hospital of New York City

THE CARE OF PATIENTS IN THE TERMINAL STAGES OF CANCER

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EXCEPTING in obscure cases which require more intensive studies and consultations with specialists, the general practitioner's diagnosis stands to be corroborated or disproven. If the results of the investigations indicate the presence of cancer, the patient is referred to a surgeon or radiologist. When satisfactory surgical relief is obtained, he seldom reports to either the practitioner or the specialist. Unfortunately, these efforts may fail and he then returns to his family physician for further advice. Again, surgery or radiation therapy is utilized. But it is from the general practitioner that the patient seeks care and encouragement in the terminal stage of the disease when all means of cure or palliation have been exhausted.

Modern surgery has attempted to cure, by radical methods, cancer situated in various organs and extremities of the body. Medical literature today cites statistics to prove the efficacy of surgical procedures, but failures out-number cures. Radium and X-ray are being used in medical practice, both as adjuncts, and, in selected cases, as the sole treatment for neoplastic conditions. Gratifying results have been obtained by each method, but as long as the etiology of cancer remains undetermined, just so long will a specific remedy or therapy go undiscovered.

The surgeon is intensely interested in the treatment of cancer in its incipiency and operable stage. Roentgen-rays and radium are frequently employed when carcinoma has no longer an operable setting. When recurrence or metastases develop, irradiation is often the only form of treatment indicated or available. Surgery being impracticable, the surgeon's responsibility is transferred to

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the roentgenologist.   Treatment with physical agents is pursued assiduously by the radiation therapist.   Striking results may be obtained.   The cases which respond and remain without evidence of disease are no longer a problem.   Those in which growth restraint occurs may be subsequently irradiated.   If recurrences become "ray-fast," growth restraint is no longer possible and further irradiation fails to control the disease.   At this time the patient is frequently returned to the general practitioner.   His responsibility and care during the terminal phase, while not a particularly pleasing task, is one which may bring comfort to the patient and earn the gratitude of relatives.

This country has many hospitals caring for chronic invalids, but excepting the few municipal institutions and charitable foundations, too little thought has been given to the care of the individual suffering with incurable cancer.   Indigent patients will depend upon social service agencies, and religious and fraternal organizations for attention.   The patient with means will have intelligent, adequate care.

Text-books and systems of surgery and monographs on radiation therapy deal optimistically with the treatment of neoplastic disease.   Few, if any, indicate or emphasize the care necessary when surgery, X-ray, or radium have failed.   The last days of the patient may be made much more comfortable both by intelligent care and medication, as well as by optimistic psychotherapy.

Many practitioners feel that the easiest way to treat these cases is to employ large doses of narcotics indiscriminately.   Their psychology is this: the end is inevitable and if the patient is continuously narcotized he is comfortable and the anxiety of the relatives is relieved.   This attitude is deplorable.   One cannot tell how long the terminal phase will last.   If it is greatly prolonged the opiate will have to be increased, so that huge amounts will finally be employed. At times the administration of such large amounts of narcotics becomes a necessity and in such instances should not be withheld. Mild hypnotics and sedatives should first be employed in minimal doses, the amount being increased when necessary.   If these drugs are no longer effectual then one may combine small amounts of codein, and finally the opium derivatives.

Sympathetic, efficient nursing care, when possible, is a great

factor in caring for patients with incurable cancer. A cheerful attendant may be of inestimable value at this stage of the disease. The meticulous care of the patient, judicious medication, and frequent, gentle surgical dressings, when necessary, are not only prerequisites for comfort, but may prevent the isolation of the individual. Friends or relatives are reluctant to remain in the room when the patient is uncomfortable or there is a noticeable odor, due either to poor personal hygiene or the discharge from affected areas. Frequent dressings diminish secondary infection and lessen the absorption of tumor toxins. These toxic products, when absorbed, add to the anemia usually present during the terminal stage of cancer. A nurse can arrange more comfortable positions for the patient, not only helping to make conditions more bearable, but preventing the development of pressure sores. Cachexia may be obviated by carefully selecting the diet and giving frequent, easily assimilated nourishment.

Surgery and radiation therapy no longer being useful, the patient and practitioner seek other means for arresting the progress of the disease or alleviating symptoms. Recently a new "serum cure" for cancer has raised false hopes among the laity in general and a few in the profession. From time to time a number of such sera, vaccins, toxins and colloidal metallic preparations have been employed for the treatment of inoperable or recurrent neoplastic disease. These constitutional remedies have been used in addition to surgery or irradiation. Many reputable and honest physicians believe in such therapy. In employing this method of treatment one must not forget that there is an individual resistance or susceptibility of very variable limits attending the use of these agents. The apparent favorable response of certain cases cannot always be ascribed to these forms of cancer therapy. Spontaneous regression and even spontaneous disappearance of tumors have been observed. Cellular extracts, antitoxins, colloidal gold, lead and selenium have been tried, but the occasional satisfactory results following the administration of these so-called "constitutional remedies" may be due to a delayed response to irradiation. More recently, the use of tuberculin has been advocated as another method for treating incurable cancer, but clinical results have not proven it to be of superior value. The Coley "combined toxin," a vaccin containing the erysipelas

streptococcus and the bacillus prodigiosus, is the most reliable constitutional agent thus far available. The favorable response, following its use, has been more noticeable in the various types of sarcoma than in carcinoma. Treatment is begun with small amounts injected subcutaneously, the dose being gradually increased. More recently, minute doses have been given intravenously and infrequently direct into the tumor. Many gratifying results have been reported, proving its value in certain selected cases. The writer has observed three patients in whom neoplastic disease has disappeared after an attack of spontaneous erysipelas.

The use of special diets has been advocated for patients afflicted with carcinoma. A practitioner in a mid-western city is attempting to cure cancer by means of a serum and a restricted diet. The serum is an unknown quantity, the doctor refusing to reveal its nature. The diet, composed of vegetables or their extractives, will not maintain body weight. Several failures following this form of treatment have applied to us for relief. We were of the opinion that the tumor had grown at the expense of the animal economy which was already affected by disease and had subsequently been further impaired by the diet. The use of this serum and diet has not been generally accepted by the profession. It would seem paradoxical to advise a restricted non-maintenance diet in the presence of a disease whose first manifestation may often be a loss in weight, a disease which late in its course frequently causes anorexia and cachexia.

In certain instances when cancer has encroached upon nerves, diathermy has been advised and practiced. Subjectively, at times, this form of treatment has proven beneficial. Cases of carcinoma of the breast having metastasis to supraclavicular nodes experience pain due to the pressure of the disease on the brachial plexus. This complication has occasionally been relieved by diathermy. However, no regression of the tumor has been noted nor would one expect such a result. Areas that have been intensively irradiated should receive diathermy most cautiously, as we feel that this procedure causes or hastens ulceration in over-irradiated skin.

The treatment of the patient in the terminal stage of cancer is often empiric. The main efforts of the practitioner should be directed toward relieving pain, improving personal hygiene, provid-

ing efficient nursing care and establishing a regimen in the hope of maintaining body weight.

Clean bed-linens and garments, frequently changed, will add comfort. Shifting the patient's position in bed will ofttimes afford relief. The use of a Gatch bed may solve many difficulties when the patient is no longer ambulatory. Pillows may be employed to maintain position or support an extremity.

Besides the use of narcotics for persistent pain, other procedures for relief may be instituted. The pressure of tumor tissue on nerves, the invasion of or metastasis to bone and large, unhealed, ulcerating areas are responsible for intense suffering. When cancerous deposits excite pain because of their contiguity to nerves or the invasion of bone, rhizotomy, nerve section or alcohol injections may be successfully utilized. The use of a plaster cast to immobilize the spine when metastases occur to vertebrae or the application of a splint or cast on an extremity when bone is involved, either before or after pathological fracture, may greatly add to the patient's comfort.

Ulcerating lesions should receive frequent, meticulous, surgical toilets. Secondary infection plays a great rôle in increasing the local and general distress. When pain persists in spite of rigid antisepsis, additional measures must be undertaken for relief. Moist dressings of boric acid or potassium permanganate may be applied. Ointments are not as satisfactory, for they tend to seal in infection and prevent proper drainage. However, certain salves may be used. Butesin picrate, obtundia or 5 per cent. cocain ointments may be employed to relieve pain. Butyn, either in solution or in ointment forms, seems to be more satisfactory than any other modern anesthetic. It is readily absorbed, the anesthesia is maintained for longer periods, its toxicity is negligible and it produces no systemic effects.

Special modified diets should be outlined, the nature and location of the cancer determining the form. Patients with intra-oral lesions require liquid or soft diets, permitting easier deglutition. The calorie content should be as high as possible because the pain caused by swallowing may limit the amount of food intake. The patient may increase his diet if, shortly before mealtime, the mouth and throat are sprayed with a weak cocain solution. Cases of carcinoma of the esophagus without gastrostomy must be maintained on a high-

calorie liquid diet. Cooked cereals diluted with cream, to which large amounts of carbohydrates, preferably lactose, are added, may be given with little difficulty. Milk, with the addition of glucose or lactose, eggs, and creamed soups may be given. One should attempt to give a diet which will approximate 3000 calories. The patient with a gastrostomy or jejunostomy may be given a similar diet. When disease does not involve the gastro-intestinal tract, a full maintenance diet should be given.

It may not be amiss to again emphasize the importance of providing efficient, sympathetic and cheerful nursing care. If, for economic reasons, a full-time attendant cannot be supplied, supervision of the case by part-time or social service nurses may be of great help. Nursing care is not infrequently of more importance than medical attention.

Measures for the relief of incurable, intra-oral carcinoma are frequently attended by many difficulties. The practitioner repeatedly finds his resources taxed in his effort to ameliorate symptoms. The use of frequent bland irrigations to check oral sepsis and relieve distress in cancer of the tongue, the floor of the mouth and the alveolar ridge will be required. Weak solutions of bicarbonate of soda, normal saline, or the combination of salt and soda are usually satisfactory. Diluted Dobel's solution and many of the alkaline mouth antiseptics can be substituted. The oral cavity should be irrigated at least every two hours, using two quarts of fluid in an irrigation can and a soft rubber tip or catheter. The stream should not be too forceful but there must be a sufficient head of pressure if satisfactory cleansing is to be obtained. Infrequently, Dakin's solution or one of its modifications can be used as a spray but with any hypochlorite solution a subsequent irrigation of saline should follow. When local pain is present, a solution of six five-grain aspirin tablets in two-thirds of a glass of water may serve as a mouth wash and gargle. For intractible pain, solutions of cocain or Butyn may be indicated, especially when food is taken. It may be necessary to employ these anesthetics before the patient will take nourishment, as the presence of food in the oral cavity may cause distress. Orthoform or cocain powder may be insufflated when nourishment is taken. If the patient is to obtain an adequate food supply the use of these anesthetics is often imperative. The diet, for the most part,

will consist of liquid or semi-solid foods. Milk and cream to which are added raw eggs and various carbohydrates, creamed soups, custard, ice cream and cooked cereals form the main part of such a diet. Fats may be supplied by the inclusion of olive oil or melted butter in the milk and creamed soups. For the relief of local and general pain, the oral administration of drugs can be continued as long as possible. Combinations of codein, aspirin, pyramidon or cibalgin, in tablet or liquid form, are given. Many times it will be thought preferable to employ codein or morphin hypodermically. For intense pain, hypodermics or pantopon or Schlesinger's solution may be necessary for relief. When intra-oral cancer has invaded bone, especially the mandible or maxilla, alcohol injections are indicated. The blocking of the second and third branches of the trigeminal nerve, by the injection of 95 per cent. alcohol, will frequently bring about complete relief. Satisfactory results usually follow this procedure and its use is to be highly recommended.

There are two important problems in caring for patients with cancer of the larynx in its terminal stage. The first is to outline a high-calorie liquid diet which can be taken with minimal discomfort. The other is probably of equal importance: to institute therapeutic measures which will lessen cough and dyspnea. Most patients with incurable laryngeal carcinoma have been tracheotomized. As a rule, these cases experience pain only during deglutition. With such severe discomfort gastrostomy may be indicated to relieve this complication and to facilitate feeding. Codein and small amounts of morphin or heroin may be prescribed to control cough. If these fail, a few drops of a weak cocain solution may be introduced into the trachea. Medicated steam inhalations may be tried for the relief of cough before resorting to the administration of drugs. A tracheotomy tube of appropriate size and shape, carefully adjusted, and kept free of secretion, will make the situation more tolerable. Irritation of the skin of the neck can be prevented by suitable dressings.

Primary and metastatic cancer of the lung cause pain, cough and respiratory distress. The treatment of pulmonary carcinoma by radiation therapy, in the light of our present knowledge, is at best only palliative. It is certainly the only rational method of therapy for metastatic carcinoma of the lung. Radical surgery for primary

carcinoma of the lung is attended by a high mortality. But the treatment of most of these patients becomes purely symptomatic when irradiation can no longer be used. Pleural effusions should be aspirated by thoracentisis, affording relief from pain, dyspnea, and ofttimes cardiac embarrassment. When pain persists in spite of the complete drainage of the hydrothorax, opiates are necessary. The size of the dose will depend upon the severity of symptoms. Heroin is the respiratory sedative of greatest value but unfortunately it has been eliminated from the pharmacopeia.

Neoplastic disease of the esophagus, by reason of its interference with the ingestion of food, requires gastrostomy for the prolongation of life. Dehydration will not occur if sufficient quantities of fluid are administered. A high-calorie liquid diet, previously outlined, given in frequent, moderate amounts, is the important problem with which the practitioner is concerned.

Incurable cases of carcinoma of the stomach include those which recur following partial or subtotal gastrectomy, and the primarily inoperable ones, which have had a palliative gastroenterostomy or no operation. In either instance it may become necessary to perform a jejunostomy to feed the patient. If this additional operation is unnecessary, oral feeding can be continued with a high-calorie liquid diet, giving small amounts at frequent intervals. Cases with nausea and gastric retention may require repeated gastric lavage, using a warm soda bicarbonate solution. Achlorhydria is usually present in patients with gastric cancer and the administration of dilute hydrochloric acid and pepsin thrice daily may not only improve the digestion but may, at times, relieve gastric distress. Many of these patients loose small amounts of blood from ulcerating lesions. One should attempt to control bleeding by the use of the newer hemostatics. With severe hemorrhage, diet should be eliminated by mouth and nutrient enemata given. Transfusions may be resorted to, to make up the amount of blood lost and to prevent further bleeding. Styptics, such as silver nitrate, are of little avail in combating gastric hemorrhage. Orthoform, in powder or tablet form, and weak cocain solution may be prescribed orally for the relief of pain. When definitely indicated, narcotics should be given hypodermically.

Primary and secondary involvement of the liver and bile pas-

will consist of liquid or semi-solid foods. Milk and cream to which are added raw eggs and various carbohydrates, creamed soups, custard, ice cream and cooked cereals form the main part of such a diet. Fats may be supplied by the inclusion of olive oil or melted butter in the milk and creamed soups. For the relief of local and general pain, the oral administration of drugs can be continued as long as possible. Combinations of codein, aspirin, pyramidon or cibalgin, in tablet or liquid form, are given. Many times it will be thought preferable to employ codein or morphin hypodermically. For intense pain, hypodermics or pantopon or Schlesinger's solution may be necessary for relief. When intra-oral cancer has invaded bone, especially the mandible or maxilla, alcohol injections are indicated. The blocking of the second and third branches of the trigeminal nerve, by the injection of 95 per cent. alcohol, will frequently bring about complete relief. Satisfactory results usually follow this procedure and its use is to be highly recommended.

There are two important problems in caring for patients with cancer of the larynx in its terminal stage. The first is to outline a high-calorie liquid diet which can be taken with minimal discomfort. The other is probably of equal importance: to institute therapeutic measures which will lessen cough and dyspnea. Most patients with incurable laryngeal carcinoma have been tracheotomized. As a rule, these cases experience pain only during deglutition. With such severe discomfort gastrostomy may be indicated to relieve this complication and to facilitate feeding. Codein and small amounts of morphin or heroin may be prescribed to control cough. If these fail, a few drops of a weak cocain solution may be introduced into the trachea. Medicated steam inhalations may be tried for the relief of cough before resorting to the administration of drugs. A tracheotomy tube of appropriate size and shape, carefully adjusted, and kept free of secretion, will make the situation more tolerable. Irritation of the skin of the neck can be prevented by suitable dressings.

Primary and metastatic cancer of the lung cause pain, cough and respiratory distress. The treatment of pulmonary carcinoma by radiation therapy, in the light of our present knowledge, is at best only palliative. It is certainly the only rational method of therapy for metastatic carcinoma of the lung. Radical surgery for primary

carcinoma of the lung is attended by a high mortality. But the treatment of most of these patients becomes purely symptomatic when irradiation can no longer be used. Pleural effusions should be aspirated by thoracentisis, affording relief from pain, dyspnea, and ofttimes cardiac embarrassment. When pain persists in spite of the complete drainage of the hydrothorax, opiates are necessary. The size of the dose will depend upon the severity of symptoms. Heroin is the respiratory sedative of greatest value but unfortunately it has been eliminated from the pharmacopeia.

Neoplastic disease of the esophagus, by reason of its interference with the ingestion of food, requires gastrostomy for the prolongation of life. Dehydration will not occur if sufficient quantities of fluid are administered. A high-calorie liquid diet, previously outlined, given in frequent, moderate amounts, is the important problem with which the practitioner is concerned.

Incurable cases of carcinoma of the stomach include those which recur following partial or subtotal gastrectomy, and the primarily inoperable ones, which have had a palliative gastroenterostomy or no operation. In either instance it may become necessary to perform a jejunostomy to feed the patient. If this additional operation is unnecessary, oral feeding can be continued with a high-calorie liquid diet, giving small amounts at frequent intervals. Cases with nausea and gastric retention may require repeated gastric lavage, using a warm soda bicarbonate solution. Achlorhydria is usually present in patients with gastric cancer and the administration of dilute hydrochloric acid and pepsin thrice daily may not only improve the digestion but may, at times, relieve gastric distress. Many of these patients loose small amounts of blood from ulcerating lesions. One should attempt to control bleeding by the use of the newer hemostatics. With severe hemorrhage, diet should be eliminated by mouth and nutrient enemata given. Transfusions may be resorted to, to make up the amount of blood lost and to prevent further bleeding. Styptics, such as silver nitrate, are of little avail in combating gastric hemorrhage. Orthoform, in powder or tablet form, and weak cocain solution may be prescribed orally for the relief of pain. When definitely indicated, narcotics should be given hypodermically.

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sages by malignant disease may give rise to nausea, vomiting and jaundice. In instances of obstructive jaundice cholecystenterostomy may have been performed. This procedure is often attended by a high mortality. The patients are poor surgical risks because of their lowered vitality. Fatal hemorrhage may attend or follow such an operation when icterus is extreme. Nausea and vomiting can be partially controlled by frequent gastric lavage. The use of small amounts of dilute hydrochloric acid and cerium oxalate are quite efficacious in relieving nausea and preventing emesis. The diet in these cases should be low in fat content and when nausea is present a semi-solid bland diet is better tolerated and retained than a liquid one. Jaundice when present in these cases, usually gives rise to pruritus. Solutions of bicarbonate of soda, magnesium sulphate or calamin lotion will relieve the intense itching. Carbolated vaselin can be tried but it may be necessary to use an ointment containing a local anesthetic to bring about the relief of this distressing and persistent condition.

The practitioner's great problem in the management of carcinoma of the rectum is usually the care of the colostomy. Cases which have had radical resection of the large bowel or rectum may be left with a permanent colostomy; those in which an anastomosis has been feasible may have recurrence in this area which subsequently gives rise to obstruction. The use of colostomy bags has been widely advocated and adhered to. In spite of painstaking care the odor of bowel contents can be detected. Irrigation of the proximal and distal bowel loops, when properly given, will evacuate the colon of feces and the distal portion of secretions and bowel contents which spill over. If the irrigation is thorough, the patient will probably go throughout the day without the further escape of intestinal contents. This would obviate the wearing of a colostomy bag. A gauze pad, held in place by a binder, is often more comfortable and more sanitary. Colostomy incisions often become irritated and lanolin or zinc oxid ointment can be applied on the skin surrounding the stoma. Irritation occurs more frequently when colostomy bags are worn. An attempt should be made to regulate, by diet, the consistence of the bowel content, for, if unformed, there will be an increased or constant discharge through the colostomy. Such a condition not only leads to irritation of the skin and the discomfort of the patient, but

may result in a loss of body weight. If a high-protein diet, together with a diminished fluid intake, is outlined, the stools will be formed, often remaining in the large intestine until evacuated by the irrigation. Cases of inoperable cancer of the rectum, where surgical intervention has been palliative, are frequently in pain due to the pressure of the growth upon nerves or its adherence to the pelvic wall. In such instances suppositories of opium with belladonna or the installation of olive oil containing Tr. Opii may afford relief.

Cancer of the bladder, both in males and females, is usually terminated by nephritic toxemia due to the mechanical occlusion of the ureters. There are few measures of any avail, the resulting coma mercifully terminating the disease. The same is true of carcinoma of the prostate. Cystotomy in these cases lessens discomfort before the terminal stages are reached. Suction drainage of urine from the bladder will prevent skin excoriation and improve personal hygiene. When carcinoma of the bladder or prostate invades or metastasizes to bone, opiates are indicated for relief.

Neoplastic disease of the female pelvis in the recurrent or inoperable stages causes pain due to the pressure on nerve roots and the adherence to or invasion of bone. Rhizotomy has been tried with some degree of success but the resulting invalidism following this operation may not be justified. The relief of pain will then depend entirely upon the administration of opium alkaloids. Vesico-vaginal and recto-vaginal fistulae may occur with carcinoma of the cervix, either late in the disease when inoperable or recurrent, or as a result of extensive operations. Frequent douches with alkalin solutions will partially control the irritation attendant on such complications.

The rapid accumulation of ascites occurring in recurrent or inoperable carcinoma of the ovary is distressing. Repeated abdominal paracentisis is necessary to relieve discomfort. A low-grade intestinal obstruction may be a complicating factor and can be obviated if particular attention is given to the diet. The administration of mineral oil and mild cathartics may prevent further intestinal disturbances.

Inoperable and recurrent breast cancer when manifested by local ulcerating lesions are problems of surgical dressing care. Frequent cleansing and the renewal of sterile gauze reduces infection and odor, contributing to the patient's local and general comfort.

Dilute irrigations of peroxid or boric acid and the continuous application of moist dressings are well tolerated. The use of potassium permanganate tends to reduce odor. Dakin's solution or its modifications are not only antiseptic but deodorant. Many patients with recurrent and inoperable carcinoma of the breast experience great discomfort due to lymphedema of the arm. The size of the extremity may be so increased that it is useless, becoming an encumbrance because of its weight. The interference with the circulation of blood or lymph, caused by the presence of recurrent tumor tissue in the axilla or supraclavicular space, and infrequently the superior mediastinum, is responsible for this complication. When the condition results from the pressure of involved mediastinal nodes, radiation therapy is the only measure which can cope with the situation. The presence of tumor tissue in the axilla or supraclavicular space contra-indicates the performance of the Kondoleon operation, of frequent value in postoperative surgical elephantiasis. We have seen failures follow this operation in the presence of recurrent axillary or supraclavicular disease, and good results in otherwise uncomplicated lymphedema. Diathermy may be effectual in relieving pain, but the treatment should not be vigorous if the skin has been excessively irradiated, as ulceration may ensue. Gentle massage of the arm, extending from the wrist to the insertion of the deltoid, may be given to relieve swelling. When the patient is in bed the arm should be supported on several pillows, overcoming the circulatory stagnation when the arm is in a dependent position. The hand can be elevated above the head by providing a support which the hand may grasp, thus increasing the return flow of lymph and blood from the extremity. Elastic bandages can be applied after the arm has been maintained in such a position, thereby minimizing swelling.

The treatment of metastasis to lung and liver has been indicated in a foregoing paragraph.

When cancer has metastasized to bone, the applicaiton of various casts may relieve pain. Plaster jackets can be utilized to immobilize the spine, and casts, splinting the extremities, may relieve pain in these regions when bone is invaded. The use of these appliances is at times impracticable; in such instances a Bradford frame or a fracture board may be substituted.

The almost universal success attending the treatment of skin cancer by surgery, and more especially radiation therapy, has caused the disappearance of the extensive, disfiguring lesions which were frequently seen a number of years ago. Formerly, a "rodent ulcer," occurring on the face, was not only disfiguring to the patient, but was revolting to the attendants. The rare case, occasionally observed, is primarily one requiring surgical dressings.

Lymphosarcoma and Hodgkin's disease in their terminal stages are problems of general medical management. The very varied complaints will require symptomatic treatment. Infrequently these patients develop metastatic deposits in the vertebrae, causing intense discomfort.

In general, when a surgical or radiological cure of bone sarcoma has not resulted, the practitioner is usually concerned in relieving symptoms due to pulmonary or hepatic metastases. We will assume, as in other instances, that these cases have failed to respond or can no longer be treated by radium, X-ray or "constitutional remedies." Their treatment then becomes symptomatic and one is again referred to the paragraphs touching upon the treatment of pulmonary and liver metastases.

Cases of lymphatic and splenomyelogenous leukemia in their terminal stages are general medical problems.

The care of the patient with incurable cancer presents a complexity of duties for the practitioner. A kind heart and a clear head are required. He would do well to remember an admonishment of Carlyle's: "Not to see what lies dimly at a distance, but to do what lies clearly at hand."

TOXIN-ANTITOXIN IMMUNIZATION IN ADULTS

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THE occurrence of diphtheria in two nurses within the space of four months crystallized the policy of Schick-testing all student nurses and of attempting to immunize those susceptible. This plan, begun in June 1924, has been followed consistently for the past six years with results entirely satisfactory from the practical point of view. At this stage, however, it seems advisable to review our data and to compare our results with other similar series.

Each nurse was tested by an intra-dermal injection of the diluted diphtheria toxin on the right forearm and of the heated diluted diphtheria toxin on the left forearm for control. Care was taken in each case to produce an intra-dermal wheal of the same size and depth on each side. Three readings were made at one, two, and five days after injection. Any decided variation in reaction on the right as compared to the control on the left, was read as positive. If the variation was slight it was read as doubtful ($\pm$). Pseudo-reactions and combined reactions were noted. In tabulating our results the slight, doubtful reactions were accepted with the positives, as well as the combined reactions. We began on this course because it seemed safer to immunize even those whose susceptibility to diphtheria was slight. We were early confirmed in this policy as the only nurse in this series who developed diphtheria (less than a month after a course of three toxin-antitoxin injections) had shown a slight or doubtful ($\pm$) Schick reaction. All nurses, then, who showed such positive reactions received a course of three subcutaneous injections of one cubic centimeter of toxin-antitoxin at weekly intervals.

The toxin and heated toxin used for the Schick tests and the control, and the toxin-antitoxin used for immunization were the standard products prepared and distributed by the New York City Board of Health.[1] These were kept in the refrigerator until the time for use, and in each case before the recommended expiration date.

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In May 1926, we began re-testing those who had received the toxin-antitoxin. In November 1926, we began giving a second course of toxin-antitoxin to those still showing a positive Schick. In 1927, we began retesting those receiving the second course of toxin-antitoxin. In 1928, we began giving four injections of toxin-antitoxin at weekly intervals, and in 1929, the number of weekly injections given the positive reactors was increased to five. In a very few cases a third course of toxin-antitoxin was given.

The results obtained from a clinical standpoint are most excellent. During the six years of testing for susceptibility and of immunizing there has been only one case of diphtheria among the nurses, and that one case developed less than a month after the third injection of toxin-antitoxin, therefore before immunity could be expected.

The results obtained from the point of view of reversing the previously positive Schick test have not been as striking as those obtained in children.

As shown in Table I, a total of 302 pupil nurses were tested. Of these, 216 or 68.2 per cent. were positive. But between the various groups tested there was a considerable variation, ranging from 47 per cent. for the first group to 88.8 per cent. for the last. Many of the groups are relatively small and so the figures for any one group may be misleading. The tests on the first group of forty-three pupil nurses were done when many of them had been in training for one or two years, so that the lower percentage thus obtained may indicate an immunity acquired from exposure during the time when some of the others developed clinical diphtheria.

The influence of environment and exposure to mild unrecognized infections has been repeatedly shown. Park[2] reported a variation between 72 per cent. and 16 per cent. positives in different schools in Brooklyn in tests on 30,000 children, and between 67 per cent. and 13.6 per cent. in New York in tests on 52,000 children. Lavan and Black[3] showed variations between 80 per cent. and 28 per cent. in testing 16,562 children in Kansas City. White,[4] reviewing tests on 45,319 children in Massachusetts, found 44.1 per cent. positive in the schools of Boston, and 60 per cent., 70 per cent., 80 per cent., and even 100 per cent. positives in the schools of small towns and villages.

TABLE I

Group	Preliminary Schick						Schick subsequent to first course						Schick subsequent to second course				Third course of T.A.T.	Date third course
	Number tested	Date	Number positive	Per cent positive	Given T.A.T.	Date	Number retested	Date	Number still positive	Per cent still positive of retested	Given T.A.T. second course	Date second course T.A.T.	Number retested	Date	Number still positive	Per cent still positive		
1	43	6/24	20	47	10	7/24	17	5/26	9	52.9	2	11/26	6	6/28	4	66.7	2	10/28
2	10	11/25	13	81	12	2/25	8	10/26	3	37.5	7	11/27	1	6/28	0	0		
3	17	3/25	10	58.8	0	5/25	22	10/27	9	40.9	1	11/27						
4	31	10/25	24	77.4	22	11/25	8	6/28	1	12.5								
5	15	3/26	12	80	0	4/26	10		7	70								
6	34	10/26	26	76.5	26	11/26												
7	14	4/27	11	79	11	4/27												
8	23	10/27	14	60.9	13	11/27												
9	12	3/28	9	75	9	3/28	8	10/28	4	50	6	10/28	6	2/29	0	0	1	3/29
10	33	10/28	21	65.0	20	10/28	17	2/29	5	29.4	4	10/28	2	2/29	1	50		
11	14	2/29	11	78.0	11	3/29	8	10/29	5	62.5	4	3/29	2	12/29	0	0		
12	33	10/29	29	87.9	28	11/29												
13	18	2/30	16	88.8	18	3/30	18	4/30	5	27.7	4	11/29	3	4/30	2	66.7		
Total	302		210	68.2	207		110		48	41.3	28		20		7	35	3	

Note: Groups up to 1st heavy line received three injections in each course. Groups between 1st and 2nd heavy lines received four injections. Groups below 2nd heavy line received five injections in each course. 2nd heavy line received five injections in each course.

Among adults wide fluctuations are likewise found. White found only 13.7 per cent. positives among 792 soldier patients and attendants in a government hospital as against 77.5 per cent. positives among country school teachers and 77 per cent. positives among Smith College students. Park[2] reported 16 per cent. positives among 4,396 adults in an insane asylum as against Crooks[5] with 72.6 per cent. positives among 613 nurses. O'Brien, Eagleton, Okell, and Baxter[6] found in testing the nurses of three different hospitals 50.5 per cent., 22 per cent., and 26 per cent. positives, respectively. Of Crooks's nurses, 139 of urban environment showed 51.8 per cent. positives, while 376 of rural origin showed 81.6 per cent. positives. However, among the nurses of the American hospitals the percentage of positives is fairly constant and relatively very high, as shown in Table II, with a total of 2,369 nurses tested and 63.4 per cent. Schick positive. In short, it is readily deduced that American student nurses are recruited largely from the smaller towns and villages and that even those from the cities come from the less congested districts.

By the middle of 1928 we had re-schicked sixty-five nurses subsequent to their course of three injections of toxin-antitoxin. Of these twenty-nine or 44.6 per cent. were still positive. These figures are to be compared with results in other groups tested after immunizing inoculations. Thus O'Brien and his co-workers found 24.2 per cent. still positive of sixty-two re-tested; Schroder[12] and Park, 17 per cent. of 117 re-tested; Crooks 7.7 per cent. of 156; Muslow[10] 25 per cent.; and Hooker[11] 24.6 per cent. of 171 re-tested. Of these Hooker used a 3L + mixture of toxin-antitoxin and Muslow an L + mixture; Crooks first a 3L + mixture, later 0.1L + mixture; Cooke, a 3L + mixture. However, Schroder[12] and Park found that the rate of immunization was not materially affected by using a 6L + dose, a 3L + dose or 0.1L + dose of toxin in the mixture, and that the smallest of these doses gave much less local reaction.

These results in adults are not nearly so good as in children. Park[2, 13] reported only 10 to 20 per cent. persisting positives after three injections; O'Brien, Eagleton, Okell, and Baxter 2 to 15 per cent. positive after a single course; and Zingher[14] 10 to 30 per cent. after two to four doses of toxin-antitoxin. Cooke wrote of nurses: "The number of individuals in whom the Schick reaction remained

positive after three doses of toxin-antitoxin is somewhat larger than is usually reported in children after immunization." And even in children Zingher found that the immunity response varied in different groups as much as from 21 per cent. to 75 per cent., and that the higher the percentage of susceptible children, the poorer the response to toxin-antitoxin. Likewise, even with children, Schwartz and Janney[26] found that after three injections of toxin-antitoxin there remained in varying series 15 to 38 per cent. who persisted Schick positive. They cite a series of 392 children in a suburb of Milwaukee who showed 33.7 per cent. still Schick positive after the usual course of three injections of toxin-antitoxin.

In an attempt to increase our immunity response in 1928 we began giving a series of four injections each of one cubic centimeter of toxin-antitoxin, but of thirty-three nurses so inoculated we still found fourteen, or 42.4 per cent., persistently positive. Hence, in November 1929, we began giving a series of five injections, and of eighteen nurses recently re-tested five months later, only 27.7 per cent. were positive.

As shown in Table I, twenty-eight nurses received a second course of toxin-antitoxin. Of these, twenty were re-tested four to seven months later, and of the twenty there were seven, or 35 per cent., still positive. Of this group of seven persisting positives, four had received six injections of toxin-antitoxin; one had received eight injections; and two had received nine injections. Three of these nurses were given a third course of toxin-antitoxin but no subsequent Schick test was made. Park reports occasional children who resisted two courses of toxin-antitoxin. O'Brien and his co-workers found one child who remained positive even though re-injected. Cooke found five still positive out of eight nurses who had received a second course of three injections of toxin-antitoxin and concluded that: "Certainly a few individuals appear refractive to immunization as indicated by the Schick test." This statement is well exemplified by a graduate nurse who had shown a positive Schick test in 1925, and who had received courses of toxin-antitoxin in various hospitals in February 1925, September 1925, September 1926, February 1928, and June 1929. On each occasion she had shown a persistently positive Schick. When I tested her along with the pupil nurses in February 1930, she still showed a

frankly positive reaction and I duly administered her sixth course of toxin-antitoxin. However, she believes that each succeeding Schick reaction has been less extensive than before.

It is interesting to note and most important to emphasize that the clinical results obtained in preventing the appearance of diphtheria by this process of Schick-testing and actively immunizing with toxin-antoxin are extremely good and rather out of line with the somewhat more limited reversal of the Schick test. In our series, despite the only moderate success in obtaining negative Schick tests, we had only one case of diphtheria in the six years, and that one case within a month of the attempted immunization. Hooker reported fifty-five cases of diphtheria among 265 nurses in ten years, an incidence of 21 per cent., before he started active immunization. After beginning immunization, of 270 nurses tested, only five cases of diphtheria occurred, and in two of these only one and two months respectively had elapsed since the last injection. In one case the diagnosis was somewhat doubtful as the patient had a negative Schick and may have been only a carrier with a slight sore throat. But even, if all five cases are charged against the method, the incidence is only 0.74 per cent. during the same time when non-immunized affiliated nurses developed diphtheria in about the expected proportions.

Likewise Crooks found nine cases of diphtheria among sixty-nine nurses, or 13 per cent., before prophylaxis was used. With the employment of passive immunization for those who were Schick positive, out of 298 nurses, sixteen or 5.3 per cent. developed diphtheria. With use of active immunization, five out of 191 nurses, or 2.6 per cent., developed diphtheria. If four of these cases were discounted because they had not been completely immunized, the percentage is only 0.53 per cent. Cooke[7] reported a diphtheria incidence of 28.6 per cent. among nurses on duty in the contagious pavilion in the three years preceding active immunization, while in the four years of immunization only two cases occurred, or 1.5 per cent. One of these occurred two days after the first inoculation and in the other, the diagnosis was doubtful as the patient was apparently a carrier with a sore throat. Cruikshank[15] obtained very similar results using a toxoid-antitoxin mixture.

This great improvement in the incidence of diphtheria (amount-

ing almost to a total prevention of the disease if we discount those cases that occur within a month or two of the attempted immunization and those that are apparently only cases of sore throats with incidentally positive cultures) suggests that even the cases still Schick positive have been made more resistant to the infection. Possibly, though the body does not show enough antitoxin per cubic centimeter of serum to give a negative Schick, the tissues are sufficiently sensitized to react more readily against new toxin.

The injections of toxin-antitoxin that we gave numbered 871, and were given to 208 nurses. The reactions from the inoculation of toxin-antitoxin of 0.1L + doses have been only very slight and local, with redness and soreness of the arm. In no case has the local reaction been enough to incapacitate the student nurse. In one case after injection there was a moderate fever with some generalized aches and pains which suggested a grippe infection, but as these were associated with a somewhat more severe local reaction than usually seen, the condition was ascribed to the inoculation. Even in this case the temperature was normal within twenty-four hours, and the patient on duty within forty-eight. In none of those who received a second or third course of inoculations was there any manifestation of serum sickness or urticaria, though the local reactions were often more marked.

It has been shown repeatedly that the administration of toxin-antitoxin produces a sensitization against horse serum in many individuals. Hooker[16] was the first to emphasize this hypersensitivity and recommended that some other animal than the horse be used for the production of that antitoxin destined for use in toxin-antitoxin mixtures. Crooks[17] reported a case of serum sickness in an individual who had received two courses of toxin-antitoxin two years previous to an administration of antitoxin. Seven days after, there developed marked edema and itching with syncope and cyanosis and a disappearance of the radial pulse. There were severe diffuse joint and muscle pains and a temperature that ranged up to 103°. Park[18] corroborated Hooker but decried the seriousness of the phenomenon. Stewart[19] cited seven cases in children, previously inoculated with toxin-antitoxin, who were given serum, one for prophylaxis against tetanus, and five for prophylaxis against scarlet.

Gatewood and Baldridge[20] cite one case which, given antitoxin

ten months after toxin-antitoxin, developed marked necrosis at the sites of the antitoxin injections. Stewart[21] produced anaphylaxis in guinea pigs after first sensitizing with toxin-antitoxin and then injecting diphtheria antitoxin or scarlet fever streptococcus antitoxin.

In only one of our immunized group was serum subsequently given. This individual, who had received a course of four injections of toxin-antitoxin in October 1928 and a second course of four more injections in February and March 1929, was admitted as a patient on April 15, 1930, because of a sore hroat. The appearance of the throat was clinically suspicious of diphtheria so that 10,000 units of antitoxin were given intramuscularly. Immediately after this injection there developed a marked urticarial rash over face and chest with severe itching, but adrenalin administration produced relief. One hour after, the patient complained of feeling weak and vomited. The pulse was almost impalpable, but the heart was regular, and the blood-pressure was 80/60. Adrenalin and digitan were given hypodermically. When I saw the patient for the first time, eight hours after the antitoxin was given, she showed a pallor of the skin with a bright blotchy eruption on cheeks, chest, and abdomen. The heart was not dilated; its rate was 105, and the sounds at the apex were of good muscular quality, but the blood-pressure was 80/60. With the use of adrenalin the patient gradually improved. In the course of the next few days the soreness and edema of the throat subsided, and the membrane cleared. However, five days after the intramuscular injection of antitoxin, there again appeared a giant urticaria with marked itching which required the use of adrenalin every three hours. The temperature went up to 103°, the pulse to 112, and the heart sounds were of poor muscular quality. The condition cleared up in three to four days, there was no recurrence of throat symptoms, and the cultures for diphtheria bacilli were all negative. There was no previous history of hives, asthma, or serum urticaria.

In view of Ratner's[22] recent paper denying the possibility of sensitization against horse serum by the small amounts of serum globulin in the toxin-antitoxin mixture, I might add to the abundance of evidence of such sensitization the following case which occurred in a member of my family. A child aged eighteen months received three injections of toxin-antitoxin. At the age of four years he

received a prophylactic dose of tetanus antitoxin and six days later had a typical attack of serum sickness with vomiting, temperature of 102°, and giant urticaria which subsided in about three days. He later received a prophylactic dose of human measles serum with no reaction. He has had no other attacks of hives or urticaria in the following five years, despite occasional contact with horses.

These experiences emphasize the desirability of using for the toxin-antitoxin mixture an antitoxin derived from the goat or sheep as suggested by Hooker and by Stewart, or else the use of diphtheria toxoid without serum as suggested by Larson and Elder[23] or of anatoxin as used in France by Ramon and Helie.[24] The value of Ramon's method has recently been confirmed by Dick and Dick,[25] and by Schwartz and Jauney.[26]

CONCLUSIONS

By Schick-testing all pupil nurses and inoculating with toxin-antitoxin those shown susceptible, it has proved possible in our experience of six years practically to prevent diphtheria.

We obtained a reversal of the Schick reaction in 55.4 per cent. after three injections, and in 72.3 per cent. after five injections.

It is important to re-test all those who receive toxin-antitoxin and to repeat the inoculations if the Schick reaction persists positive.

We recommend that with nurses a course should consist of five injections of one cubic centimeter of toxin-antitoxin at weekly intervals. Inasmuch as a period of two or three months must elapse after

TABLE II

Results of Schick Tests on Nurses in American Hospitals

	Number	Per cent positive
Cooke (7)	147	58.5
Rhoads (8)	64	67
Crooks (5)	613	72.6
Weaver and Rappaport (9)	115	54
Muslow (10)	97	67
White (4)	658	52.3
Hooker (11)	373	64
Lintz (present series)	302	68.2
Total	2369	63.4

the toxin-antitoxin inoculations before immunity develops, it would be desirable to have the Schick test and the injections made before the pupil nurses report for training. Then after the pupils are admitted check tests and re-tests could be made.

It is suggested that the clinical results obtained by active immunization are better than is indicated by the Schick reversal, perhaps because the tissues are sensitized against the toxin.

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POSTPARTUM FEVER*

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Introductory.—The subject of elevation of temperatures in parturient women is so enormous, and so full of portent to the human race, that in a short article such as this we can only touch on certain fundamental aspects. When we consider that almost twenty thousand women in the United States registration area die annually as a result of child-birth, and that more than one-third of this number die as a result of birth-canal infections, and when we realize that these figures have not receded appreciably in recent years, it makes us feel that the subject is worthy of all the discussion it receives, though at times there seems to be superfluous repetition. We therefore believe that, even though this article has very little of original nature to contribute, it will add the experiences of additional observers.

The frequency of puerperal fevers, even under ideal hospital conditions, may be demonstrated by the incidence in the obstetrical department of the Fifth Avenue Hospital, where, in a series of 1,694 parturient women, it occurred 196 times, or in about 11.5 per cent. of these cases. All these temperatures were not due to birth-canal infections but a large enough percentage was to constitute a matter for serious discussion.

It is to be regretted that hospitals have not arrived at a generally accepted standardization of diagnosis and statistical determinations of birth-canal infections. The methods of expression of the diagnosis of puerperal infections still remain antequated and inadequate. The terms "sepsis," "sapremia," and "septicemia" are used without any real conception of the underlying pathology. This

state of affairs is the result of a number of factors, among them being: the incomplete teaching of the subject in our medical colleges; the indifference of the physician; the difficulty in making a differential diagnosis; the lack of effective treatment in many cases; and possibly the lay conception of "blood poisoning" as a blanket diagnosis for fever resulting from confinements. Analyzing the term "sapremia," it would be taken to mean the absorption into the body of toxins liberated by the action of saprophytic bacteria upon retained products of conception, usually placenta, its differentiation from "septicemia" in the minds of many depending largely upon the severity of the symptoms produced. It is doubtful if the condition "sapremia" ever occurs, and the term "septicemia" should be reserved entirely for the condition in which bacteria are present in the blood-stream, i.e., bacteremia.

Modern medicine demands of obstetrics a more scientific, and, as a result, a somewhat more complicated classification of infections originating in, or attacking the genital tract after delivery. A plan of classification after De Lee, though somewhat modified, should consider the following factors:

1. Location, type and extent of the inflammatory lesion or lesions.
2. Portal of entry of bacteria.
3. Type of bacterial organism.
4. Presumable method of production (such as breaks in technic, instrumentation, or any type of infective invasion of the birth canal).

It is, of course, very difficult in most cases to determine all of these factors, but if we were to attempt it, we would at least have a much more acceptable form of diagnosis. Thus, we would refer to a general parametritis, resulting from acute endometritis, streptococcic, following invasion of the uterus for manual extraction of the placenta. How much more explicit such diagnosis would be than any of the more general diagnostic terms! Before proper statistical data could be gathered, some such outline of diagnosis would be necessary.

Etiology.—A study of the statistics on the infections of the past twenty-seven months at the Fifth Avenue Hospital has added

further verification to the great mass of evidence as to some etiological factors in the production of the infections. We have adopted the rule that a case is considered one of puerperal infection if, on any two takings of the temperature (by mouth), the temperature reaches 100.4° Fahrenheit, unless proven to be of other origin. Thus we eliminate from our number of cases those in which the temperature reaches this height only once and those proven to have other causes. Temperatures at the Hospital are taken every four

FIG. 1.
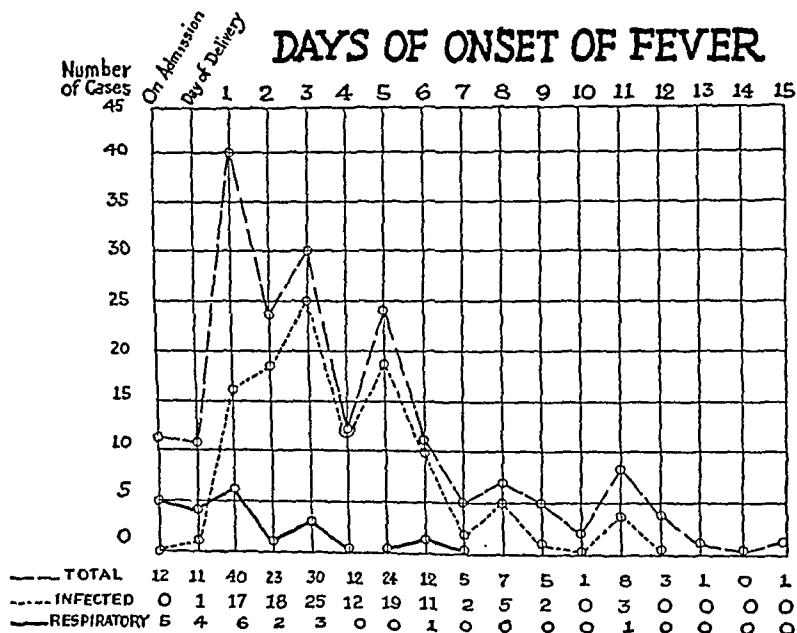
hours. In our series of 196 cases we have eliminated thirty-six cases for the first reason, and forty-five for the second, leaving a net morbidity of 115 cases of birth-canal infection, an incidence of 6.79 per cent.

The etiological factors involved may be conveniently divided into endogenous or autoinfection, exogenous, predisposing and exciting, the last representing the causative bacteria.

Endogenous Causes.—Considering the endogenous causes, we must explain the occurrence of those infections in patients in whom all the exogenous possibilities and even predisposing factors are absent. It is not impossible that the presence of a cervicitis may have

some relationship to the production of infections in these patients. The rubbing of the fetal head in its advance and regress may devitalize the cervical tissue and favor the spread of the infective material if it is present.

Again, the frequent but unavoidable lacerations of the cervix may provide the necessary portal of entry for the bacteria already present in an infected cervix. We consider it good practice to observe the cervix in all pregnant women, and treat cases of severe cervicitis

FIG. 2.

POSTPARTUM FEVERS DIVIDED ACCORDING TO CAUSE

TOTAL FEBRILE CASES	BIRTH CANAL INFECTIONS	FEVER ON ONLY ONE TAKING	RESPIRATORY	MASTITIS	PYELITIS	CYSTITIS	ENCEPHALITIS	BACTERIAL ENDOCARDITIS	INFECTIVE DERMATITIS
196	115	36	17	10	8	7	1	1	1

No. of Cases

ELIMINATED
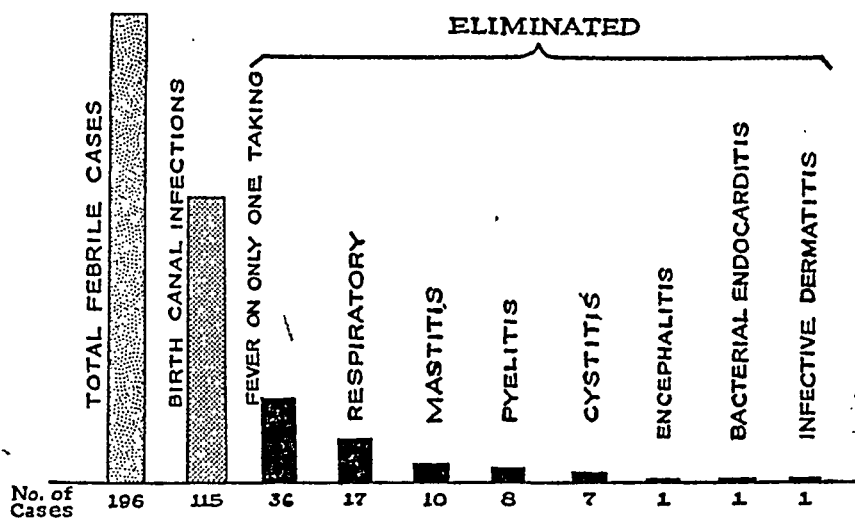
with the idea of perhaps preventing this type of infection of the birth canal.

It has been stated that a chronic or subacute inflammatory lesion of the pelvis may flare up during the early puerperium, so this also may be added as a possible endogenous cause.

Remote infective foci being present are probably not causative in themselves of puerperal infections but may contribute as a devitalizing element.

Exogenous Causes.—Exogenous causes are undoubtedly more commonly responsible for birth-canal infections, and most important among these is the attendant, either physician or midwife. It is

here that we must stress the importance of surgical technic in the handling of obstetrical cases, no matter under what environment the delivery occurs. In our hospital technic the methods of the operating room are strictly adhered to, and there is no reason why at home the same technic, modified if necessary, cannot be carried out.

FIG. 3.

INCIDENCE OF PUERPERAL INFECTION ACORDING TO PARITY
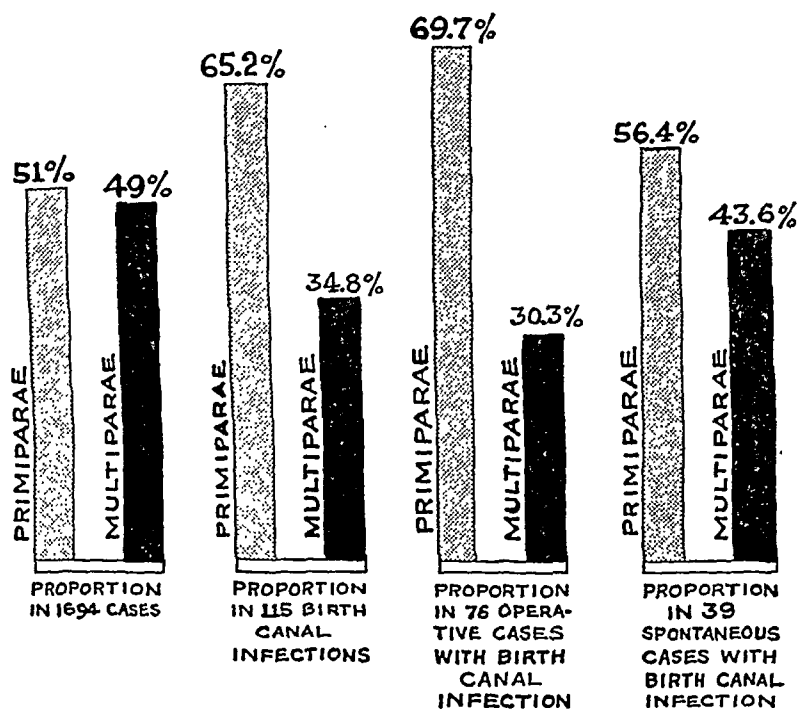
Nothing unsterile should come into contact with the operative area (vagina and vulva) at any time during labor. It is a sad commentary that in home deliveries the midwife seems to fare better in this respect than the physician, from whom we should expect more.

Vaginal examinations are performed more frequently than necessary in many instances. They should be cut down to an absolute minimum, and the attendant should pause before performing one to determine if the need therefor exists. In the series of cases here presented, vaginal examinations were done on the average of .8

per patient. Forty of the 196 patients with fevers had no internal examinations, and the largest number done in any case was three, and this frequency occurred in only eight cases in the series. Rectal examinations were done only twenty-six times in a total of eighteen patients.

Fig. 4.

PUERPERAL INFECTION IN RELATION TO OPERATIVE PROCEDURES

TOTAL CASES	INFECTED	PERCENTAGE INFECTED
2	1	MANUAL EXTRACTION OF PLACENTA — 50%
44	13	CESARIAN SECTION — 31%
22	5	UTERINE PACKING — 23%
24	5	VERSION — 21%
5	1	MANUAL DILATION OF CERVIX — 20%
14	2	HYDROSTATIC BAGS — 14.3%
535	48	FORCEPS — 9.1%
23	1	BREECH EXTRACTION — 4.1%
669	76	AVERAGE OF OPERATIVE CASES — 11.38%
1694	115	INCIDENCE IN ALL CASES — 6.79%

Coitus in the latter part of pregnancy is obviously capable of producing infections in the puerperal period, and it is therefore necessary to inform the patients of this fact as they often do not know of its harm. Handling of the genitals, tub bathing and douching are also to be warned against in the latter part of pregnancy. There are times when douching is the choice of a lesser evil, such as cases in which there is a profuse discharge resulting from vaginal or cervical infection. It is our practice to give our patients written

instructions for their behavior, diet, *etc.*, during their pregnancies, and the above points are stressed therein.

The environment is also a factor in the production of these postpartum infections. It is claimed by some that the occurrence of infections is less frequent in home deliveries because of the immunity of the patient to organisms in her own home and because of the reduced likelihood of transmission of infection from other patients

FIG. 5.

INCIDENCE OF PUERPERAL INFECTIONS IN FORCEPS DELIVERIES

	HIGH	MEDIUM	LOW	Average Forceps	Entire Series
	15.4%	14%	6.7%	9.1%	6.79%
No. of Cases	26	136	373	535	1694
Infected	4	19	25	48	115
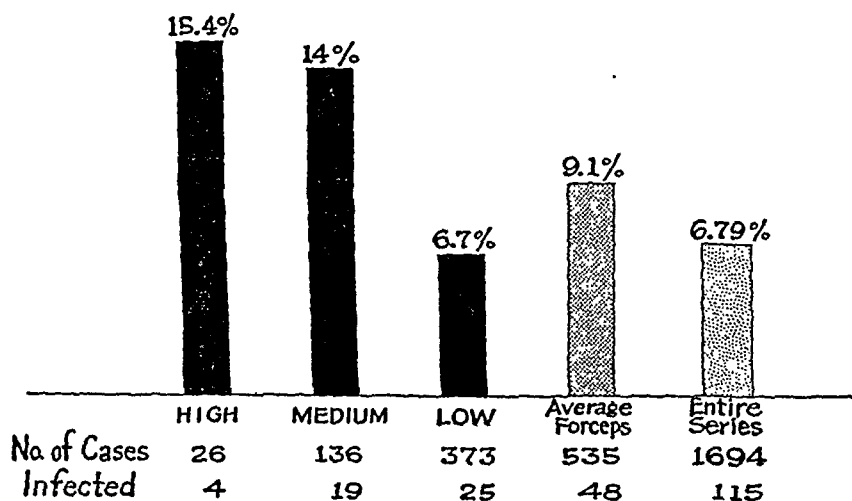
as in hospitals. It is also claimed by some that the danger of infection is increased for cases in general hospitals, but that it is decidedly lessened in maternity hospitals. We are rather inclined to feel that it depends to a large extent upon the hospital. The Fifth Avenue Hospital is a general hospital, and our obstetrical patients are under the same roof as infected medical and surgical cases, but the maternity floor is completely isolated from the surgical and medical floors. Our patients are all in single rooms, each with a lavatory and a complete set of utensils, such as wash basins, bed pans, *etc.* Actively infected cases are removed from the floor and we therefore feel that we can secure all the isolation that could be obtained if our patients were in an entirely separate building.

Predisposing Causes.—In discussing the predisposing causes we believe we have some very interesting statistics which we shall present as we consider these causes.

We must first understand that in dealing with obstetrical cases we are confronted with a surgical wound, presenting in some ways more serious aspects that the average surgical case. The wide open placental area with large vascular sinuses inviting infection, the danger of retention of placental tissue, and the frequent exhaustion

FIG. 6.

INCIDENCE OF MASTITIS POSTPARTUM
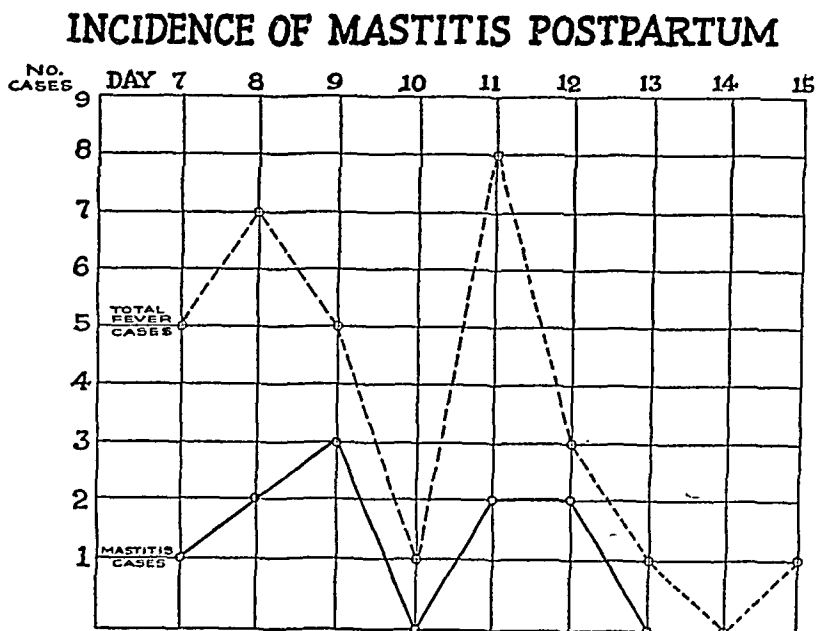
of the patient from her labor, along with a greater or lesser loss of blood, are some of the more serious conditions present. On the other hand, the free drainage of the uterine cavity, its contractile ability, the relatively infrequent need for introduction of hands or instruments into its cavity are some of the brighter aspects of the situation.

So we must consider that pregnancy itself is one of the important predisposing factors.

Prolonged, exhausting labor is a very decided factor by reducing the resistance of the patient, as is the excessive loss of blood. Retention of placental tissue, as stated before, creates an excellent culture medium for bacteria and may also be added as a predisposing cause.

Primiparity also appears to predispose to postpartum infection. In the series of 115 cases, 65.2 per cent. were primiparae and 34.8 per cent. multiparae, whereas in the entire series of 1,694 cases, 51 per cent. were primiparae and 49 per cent. were multiparae, showing a considerable increase in the infective incidence in primiparae. This probably can be explained on the basis of the greater likelihood of exhausting labor, the more frequent need of operative interference and the increased incidence of laceration.

The relation of entry of the uterus during labor, at delivery, or shortly after delivery, and the liability to postpartum infection of the birth canal, would best be illustrated by the following table of operative procedures. The list includes only the types of cases in which the uterus is invaded by hand or instrument.

Operative Procedure	Total Cases for Entire Series	Cases with Postpartum Infection	Percentage of Operative Cases with Postpartum Infection
Forceps................	535	48	9
Caesarean section......	42	13	31
Breech extraction.......	23	1	4.1
Version...............	24	5	21
Uterine packing........	22	5	23
Manual dilatation of cervix.................	5	1	20
Hydrostatic bags.......	14	2	14.3
Manual extraction of placenta...............	2	1	50
Curettage for retention of placenta..........	1	0	0
Totals................	668	76	Average per cent. 11.38

The above figures make the greater frequency of infections following the invasion of the uterus an evident matter, and we have therefore substantial evidence of such instrumentation and maneuvers as a factor in the production of infections.

Because of a very interesting deduction we can draw we are presenting below a table showing the incidence of puerperal infections in the various degrees of forceps deliveries.

	Total Cases in Series	Cases with Puerperal Fever	Percentage of Cases with Puerperal Fever
High forceps............................	26	4	15.4
Mid forceps.............................	136	19	14.0
Low forceps.............................	373	25	6.7

It is the usual practice of the greater number of members of our staff to use the low forceps "electively" or "prophylactically," believing a large part of the perineal stage may be saved mother and infant with benefit to both. As a consequence, it is gratifying to note that the fever incidence of low forceps is slightly lower than that of cases in general, both spontaneous and operative, that is, 6.7 per cent. as against 6.79 per cent.

However, we do not wish to have this construed as a recommendation for the general use of forceps for this purpose, as we believe that two conditions are absolutely essential for the successful performance of the procedure: first, the operator should be thoroughly qualified; and, secondly, the delivery room and technic should be the equivalent of hospital conditions.

Of the thirty-nine cases in which birth-canal infections developed but delivered spontaneously without instrumentation, twenty-two were primiparae and seventeen were multiparae, 56.4 per cent. and 43.6 per cent. respectively.

Lacerations of different types also predispose to infections but to an extent these can be controlled. The application of forceps or performance of version through an undilated cervix certainly increases the likelihood of cervical laceration, as does the performance of "manual dilatation," which operation we are proud to relate was performed in only five cases in the entire series. Only seven of the temperature rises resulted from infections of the perineum, of which four followed lacerations and three followed episiotomies.

Diagnosis.—The pathologic diagnosis causative of temperatures postpartum presents a study deserving of our consideration, and here again we give some of the statistics in our series.

The preponderance of cases eliminated as not due to birth-canal infection were respiratory, pyelitis and mastitis, as shown by the figures presented below:

Respiratory	17
Mastitis	10
Pyelitis	8
Cystitis	7
Encephalitis	1
Bacterial endocarditis	1
Infective dermatitis and "ptomaine"	1

It is interesting to note that fifteen of the respiratory cases were either admitted with their conditions or developed them within forty-eight hours of delivery, and that nine of the cases of mastitis developed on or after the eighth day postpartum. These facts have a certain amount of diagnostic value, as will be discussed later.

The following table indicates the day of onset of fevers for the entire series:

Day	On Admission	Day Delivery	1	2	3	4	5
No. cases............	12	11	40	23	30	12	24
Day	6	7	8	9	10	11	12	13	14	15
No. cases........	13	5	7	5	1	8	3	1	0	1

The diagnoses of cases with elevated temperature on admission were: respiratory, in five cases; pyelitis, in one; toxemia of pregnancy, in one; bacterial endocarditis, in one; and in four, no diagnoses could be made.

The cases with fevers commencing on the day of delivery were diagnosed as: respiratory, four; cystitis, two; pyelitis, one; and three remained undiagnosed. The remaining case continued its temperature and was later diagnosed as "septic" parametritis.

Of the forty cases developing fevers on the first day postpartum, seven were respiratory, nineteen undiagnosed, and two were post-Cesarian, one of which died of a purulent peritonitis and the other developed a fecal fistula. Four were birth-canal infections and the others were divided among numerous causes.

Of the 102 temperatures commencing from the second to the sixth days postpartum, eighty-five, or 83⅓ per cent., resulted from infections of the birth canal.

From the seventh day on, aside from the cases in which the diagnoses were unknown, the majority were due either to mastitis or phlebitis. The table below indicates the frequency of the above:

Day	Total Fevers	Mastitis	Phlebitis
7..	5	1	2
8..	7	2	0
9..	5	3	0
10.......................................	1	0	0
11.......................................	8	2	2
12.......................................	3	2	0
13.......................................	1	0	0
14.......................................	1	0	0

The element of the time on onset of elevated temperature, as evidenced by the above figures, is an important one in the establishment of a diagnosis.

The frequency of respiratory infections causing elevations of temperatures on the day of delivery and the day following may result from exposure (the patients perspiring invariably throw off covers during labor) plus lowered resistance due to labor and to the use of general anesthesia.

It is usually not a difficult task to differentiate these respiratory temperatures from those resulting from birth-canal infections, so no detail of this subject will be related.

The large number of temperatures commencing from the second to the sixth days and originating in the birth canal suggest a brief résumé of the distinguishing features of each type.

Perineal infections are usually easily recognized. Fever, plus pain, edema, tenderness and redness of a repaired perineum, accompanied by the discharge of pus upon the removal of sutures, or oozing between sutures, make the diagnosis evident.

Endometritis, which is the most common lesion encountered, manifests itself by fever and accelerated pulse, sometimes preceded by a chill, and boggy, poorly involuted uterus. The lochia are usually altered, usually lessened, especially where the streptococcus is the predominating organism. The exudate is frequently abundant and purulent when the colon bacillus predominates. Metritis cannot be considered a separate entity, and it follows and accompanies endometritis. Pain and tenderness are complained of particularly in metritis, in addition to the usual signs of endometritis.

Parametritis produces a marked edema of the subperitoneal connective tissue. On vaginal examination there is at first a firm swelling of the tissues about the uterus and the uterus is fixed in the mass. If the lesion is unilateral, the signs are, of course, one-sided, and the uterus may be displaced toward the opposite side. Later, upon palpation, there is a putty-like feel of the edematous tissue, which gradually resolves. Tenderness and pain may be marked in the early stages but these subside as reabsorption takes place. Pus formation is relatively uncommon.

Salpingitis as a secondary lesion rarely occurs, but when it does, suppuration is common. Unlike gonorrheal salpingitis, it is

more likely to be unilateral, and is characterized by the fluctuating tube mass.

Peritonitis in less serious cases, which fortunately constitute the greater number of cases, is located in the pelvis and limited to the visceral peritoneum about the uterus and broad ligaments. There is some lower abdominal rigidity with slow progress and regress of the condition. In the general peritonitis cases, the infection gains access to the peritoneum through the uterine lymphatics, or as a result of the rupture of an infected viscus or abscess. The onset of general peritonitis postpartum is sharp, the course stormy, and it is usually rapidly fatal. It is characterized by the usual general rigidity, tenderness and distention, vomiting, fever and very high pulse rate. Finally, the temperature may drop, the pulse become extremely rapid or even imperceptible, until death supervenes.

Bacteremia depends for its positive diagnosis upon a positive blood culture. The presence of an infective focus (such as an endometritis) followed by chills, further elevation of temperature, sweats and greatly accelerated pulse suggest its probability. Some cases of bacteremia are rapid, the blood-stream involvement occurring before a local focus can be diagnosed. Others are slower in onset, and are likely to be less serious than the latter.

Pyemia is a very rare complication and involves the lodgment of septic emboli in different regions of the body. The "showers" of bacteria into the blood-stream are accompanied by chills and acute rise in temperature. The prognosis in these cases is also grave.

Pelvic thrombophlebitis is rather late in its onset (after the seventh day) and may commence with a chill, fever and rapid pulse. Pain may be experienced and the thrombosed veins may be felt in many cases, but at times are not palpable. The uterus and adenexa otherwise seem perfectly normal as a rule.

Subsequent to the seventh day the incidence of mastitis and phlebitis of the extremities are to be considered. Mastitis is easily overlooked. It usually occurs in a patient who has had cracked nipples, so complaints of pain in the breast may go unnoticed. It is surprising how high the temperature may go with only a slight blushing of the skin in an infected area of the breast. This area is almost always confined to one quadrant or another of the breast and is always tender to touch. Abscess formation commonly occurs

within forty-eight to seventy-two hours, unless treated by temporary weaning of the infant.

Phlebitis of the extremities is usually rather obvious involving temperature and pain in the affected limb. The physical findings reveal the usual doughy feel of edema of the extremity, and tenderness over the inflamed vein. This tenderness is usually first in the region of Poupart's ligament, as the femoral vein is the one most commonly involved, and later down the leg over the tributary veins which have become involved. Phlebitis of the lower limbs always occurs late in the puerperium, from the seventh to the twenty-first day. The more severe signs persist for about a week and then disappear gradually.

Pyelitis occurs often enough to require its differentiation from birth-canal infections. Characteristically, it is ushered in by a chill, high temperature, pain in one side of the lumbar region and pain on or frequency of micturition. It may occur at any time in the puerperium and is also very common during pregnancy. Physical examination reveals tenderness and rigidity of one costovertebral angle, rarely both. The diagnosis is clinched by obtaining a positive culture and finding pus-cells in a sterile catheterized specimen of urine. It must be borne in mind that all these signs and symptoms are not invariably present.

Mortalities.—It may be interesting to note that in the 196 febrile cases discussed here, there were three deaths:

One was the case of bacterial endocarditis which was superimposed upon an old rheumatic endocarditis. This patient died about seven weeks after delivery. A positive blood culture was finally obtained about two days before death, and showed streptococci.

The second case was one following hysterectomy for a fibroid. The patient had recovered from a Cesarian delivery and four weeks later had her second laparotomy and died the following day, probably from shock.

The third case was one of purulent peritonitis. A cesarian section was performed upon this patient for pelvic disproportion following a twenty-four-hour test of labor. The membranes had been ruptured for six hours before operation. On entering the uterus, the fluid was particularly offensive in odor, and this presumably indicated a preëxisting infection. Two days later the incision was reopened

to liberate a large quantity of pus, which issued from the peritoneal cavity. The patient died a few hours later.

CONCLUSIONS

1. There is need for a satisfactory and uniform classification of diagnoses of puerperal fevers.
2. There is also need in hospitals for uniform and accurate statistics upon this subject.
3. Many puerperal fevers are preventable.
4. The following have been shown by the statistics presented to predispose to puerperal infections:
   (a) invasion of the birth canal by hands or instruments;
   (b) primiparity.
5. Infrequent, properly performed vaginal examinations do not predispose to puerperal infections.
6. Low forceps deliveries in our series of cases do not predispose to birth-canal infections postpartum.
7. A large percentage of temperature elevations present on admission or commencing within forty-eight hours of delivery were due to respiratory infections.
8. 83⅓ per cent. of fevers commencing from the second to the sixth days postpartum are due to infections of the birth canal in our series of cases.
9. The great majority of cases of mastitis and phlebitis of the extremities were shown to commence after the seventh day postpartum.
10. Pyelitis in the puerperal period occurs frequently enough to require its exclusion as a diagnostic possibility in all puerperal fevers.

ALLERGIC PURPURA

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A PERUSAL of the literature on the subject of purpura brings to light a variety of theoretical discussions concerning etiology and grouping. Almost every other author reserves for himself the right to suggest a new classification. The tendency at the present time is to revert to the classification offered by Leloir[1] in 1884. He distinguished two types of purpura: (1) "purpura par modifications du sang," and (2) "purpura par modification des vaisseaux." If we restate this in terms of modern hematology, we may divide the purpuras into two main groups:

(1) purpura characterized by a reduction in the blood platelets,

(2) purpura due to changes in the blood-capillaries.

Purpura Characterized by Reduction in the Blood-platelets.— This group of purpuric disorders is designated under various names among which purpura hemorrhagica and thrombocytopenic purpura are the most prominent. Characteristic of this condition are hemorrhages into the skin and from the mucous membranes, which frequently are severe and even fatal. The blood-platelets are markedly reduced in number, often below 35,000. There is a marked increase in bleeding time, and generally an absence of clot retraction. Coagulation time is within normal limits, and in some cases a deficiency in fibrinogen can be demonstrated. The disease runs either an acute or a chronic course, and the chronic form may be intermittent in character so that during remissions the blood findings are normal. The deficiency in blood-platelets (thrombocytopenia) is the cardinal factor responsible for the hemorrhages. Kaznelson[2] is of the opinion that the platelet reduction is due to their destruction in spite of a normal production, a process similar to the one seen in hemolytic icterus. According to Frank,[3] this reduction is due not to platelet lysis, but to a lack of platelet production in the bone-marrow. This results from some toxic process in the bone-marrow which affects the megakariocytes, the mother cells of the platelets. It is quite

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possible, however, that both factors are involved to a greater or lesser degree. Duke[4] has demonstrated that diphtheria toxin and benzol in large doses are poisonous to the bone-marrow and cause a marked fall in the platelet count. He thinks that the platelets themselves are also affected by these agents, and that this factor may contribute to their reduction in numbers. Julianelle and Reimann[5] produced purpura and a profound thrombocytopenia in white mice, rabbits and guinea pigs with injections of pneumococcus extracts. Their evidence indicates that the platelet reduction is accomplished by some action other than lysis alone. The lytic action is prevented *in vitro* by heating the extract, but the heated extract still causes purpura. Whether or not the platelets are also qualitatively altered, and to what extent capillary trauma plays a rôle in the production of the bleeding, are problems that remain to be solved. This type of purpura is called essential or primary when there is no known etiology, and secondary or symptomatic when it occurs in the course of some other disease process, such as leukemia or aplastic anemia, and following benzol and arsenical poisoning.

A hereditary variety of purpura, characterized by moderate bleeding from mucous membranes as well as purpura and ecchymosis, has also been described. Unlike hemophilia, however, both males and females are susceptible, and the disease is also transmitted by males. This group is rare and in the cases reported the blood findings are inconstant. The blood-platelets may be normal in number, but a temporary thrombocytopenia also occurs. Bleeding time is increased and coagulation time, though generally normal, is considerably prolonged in some cases.[6, 7] The retractility of the clot is impaired to a degree varying from slight delay to entire absence. Glanzmann,[8] who has designated this group as hereditary hemorrhagic thrombasthenia, believes that functional and structural abnormalities in the platelets, even in the presence of numerical sufficiency, account for the clinical picture.

Purpura Due to Changes in the Blood Capillaries.—The type of purpura that is dealt with in this paper belongs to this group. The nomenclature employed in the literature is very confusing. It has been called purpura rheumatica, purpura abdominalis, Schoenlein-Henoch's purpura, anaphylactoid purpura, hemorrhagic capillary toxicosis, non-thrombocytopenic purpura and allergic purpura.

In view of the fact that every phase of the subect of hypersensitiveness is involved in a mass of active controversy, it is advisable before proceeding further to define the limitations of the terms used. Coca[9] defines hypersensitiveness as a susceptibility in man and animal that is mediated by a special mechanism, the existence of which is indicated either by the absence of the sensitiveness in most individuals of the same species, or by its total absence in other species. Wells[10] uses the term allergy to cover all variations in reaction of living tissue to foreign chemical agents, whether antigenic or nonantigenic in character, whereas anaphylaxis is limited to hypersensitiveness which depends upon a true antigen-antibody reaction. It is not necessary for the purposes of this communication to review in detail the merits of the various classifications of hypersensitiveness. As the term allergy is generally used today, it includes all varieties of hypersensitiveness except true experimental anaphylaxis. Hence, in associating purpura with allergy, there is no implication that purpura is an anaphylactic phenomenon.

CASE REPORTS

CASE I.—M. P., female, aged twenty-nine, admitted to the Fifth Avenue Hospital May 7, discharged May 27, 1928. Her chief complaint was pain in the legs and knees. She gave a history of poliomyelitis seventeen years ago, which left her with a moderate atrophy of the right leg, but with no paralysis. Three months before admission, following child-birth, she developed edema and erythema of the face which came and disappeared intermittently. Two months later the face was free from lesions, but a similar condition appeared on the trunk. At the same time, the knees and ankles became red and swollen, and an erythematous eruption was observed on the legs.

Physical examination showed a purpuric eruption with scattered ecchymotic areas over the legs and thighs. The ankles were swollen and showed large erythematous patches. Both ankles and knees were quite tender. The tonsils were hypertrophied and cryptic. The heart and lungs were apparently normal. Blood-pressure—systolic, 110; diastolic, 75. The neurologic status revealed a moderate amount of left facial weakness. There was a positive Hoffman in the left hand. The left abdominal reflexes were absent. Left ankle clonus and a left Babinski were present. The optic fundi were normal. These findings were interpreted as being due to a small hemorrhage in the right internal capsule. The laboratory reports revealed nothing significant. Blood-count—hemoglobin, 98 per cent.; erythrocytes, 5,100,000; leukocytes, 9,000; polymorphoneutrophils, 65 per cent.; lymphocytes, 33 per cent.; mononuclears, 2 per cent.; blood-platelets, 180,000. Coagulation time varied from 4 to 6 minutes; bleeding time, 1.5 minutes; blood and spinal fluid Wassermann tests, negative; colloidal gold reaction, negative; blood urea nitrogen, 14 milligrams per 100

cubic centimeters; phenolsulphonephthalein output, 58 per cent. The urine contained a very faint trace of albumin, a few white blood cells and no casts.

The patient was kept in bed, and after one week the skin lesions subsided, only to reappear almost immediately, when she was allowed to get out of bed. This phenomenon was repeated on several occasions. During her residence at the hospital, she also developed transitory urticarial lesions on the chest and arms. The temperature remained normal throughout. A tonsillectomy was performed under local anesthesia without any undue bleeding, and was followed by an uneventful convalescence. At the time of her discharge, the skin lesions and joint pains had all cleared up, but there was no change in the neurologic status. When seen one month later, she reported that she had been entirely free from symptoms during this interval, excepting occasional small urticarial wheals on her legs. No further observations could be made, as the patient failed to present herself for follow-up and could not be traced.

Summary.—A case presenting joint pains, angioneurotic edema, erythema, urticaria, purpura and cerebral hemorrhage.

CASE II.—B. G., female, aged twenty-three, admitted to the Fifth Avenue Hospital February 29, discharged March 3, 1928. This patient was sent to the Surgical Service of the Hospital from the Out-patient Department with the diagnosis of acute abdomen. Four days previously she had developed nausea, vomiting and acute pain in the left side of the abdomen. These symptoms lasted twenty-four hours and then disappeared. Twenty-four hours thereafter, she began to have pain in both shoulders and feet, and the abdominal colic also returned and persisted to the time of admission. Physical examination showed spasticity and tenderness over the left side of the abdomen at the level of the umbilicus. The ankles and shoulders were tender, but not red or swollen. The skin over the trunk showed numerous urticarial wheals, large patches of erythema and a few scattered purpuric lesions. There was no pruritus. The examination otherwise revealed nothing of importance. The temperature was not elevated. Blood-count—leukocytes, 10,400 per cubic millimeter; polymorphoneutrophils, 76 per cent.; lymphocytes, 20 per cent.; mononuclears, 4 per cent. Urine analysis—negative, except for a very faint trace of albumin.

Immediately after admission, the patient was given a hypodermic injection of five minims of a 1 to 1000 solution of adrenalin chlorid. About ten minutes later, the pain in the abdomen was markedly relieved, and there was a definite recession in the skin lesions. Within one hour the abdominal pain was completely gone, and twenty-four hours subsequently the skin lesions and joint pains also disappeared. Following the adrenalin injection, she was given ephedrin sulphate, three-eighths of a grain three times daily, up to the time of discharge. She remained under observation for a period of two years, during which time there was no recurrence of her symptoms.

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diarrhea with mucosanguinous stool; (3) swollen and painful joints. Occasionally there are hematuria and evidences of a hemorrhagic nephritis. Hemorrhagic lesions may also occur in the meninges, brain, pleura, pericardium, bladder and uterus. The mode of onset varies. It may begin like a febrile disease with general malaise, anorexia and a mild temperature, but the gastro-intestinal symptoms, skin lesions or joint pains may be the first manifestations. There is no definite rule as to the duration of a single attack, which may vary from one to ten days, or may last a much longer period. Characteristic are the relapses which come in rapid succession after the initial attack, or at indefinite periods during many months or years.

Skin Lesions.—These are versatile in character and resemble the skin lesions described under the various allergic disorders. They consist of all varieties of purpura, urticaria, angioneurotic edema, erythema, erythema multiforme and erythema nodosum. Rarely, areas of actual necrosis are also present. Any one, or various combinations of these skin eruptions may be seen in the same patient during an attack, or the skin lesions may differ in the different attacks. Pruritus is commonly present. Purpura is generally not a prominent symptom and is frequently absent. The skin, according to Frank,[11] is sensitive to intracutaneous injections of substances such as casein or tuberculin, which will produce extensive hemorrhagic infiltrations at the site of injection. The tourniquet test is positive, and results in a small purpuric eruption, or a combination of purpura and urticarial wheals. Occasionally the lesions on the extremities are of an orthostatic nature (Case I), *i.e.*, they disappear when the patient is kept in the horizontal position for some time, only to reappear when the patient becomes ambulant.

Gastro-intestinal Lesions.—The gastro-intestinal symptoms consist of colicky pains, nausea, vomiting, diarrhea and mucosanguinous stools. Anatomically, the counterpart of the skin lesions is also found here. Edema, serous exudate, hemorrhage, and in the severe cases, necrosis occur. Partial or complete intestinal obstruction, hemorrhagic ulcers of the bowel, and suppurative peritonitis resulting from perforated ulcers have been described.[12] Likewise, intussusception is occasionally encountered. These lesions occur in any of the layers of the intestinal wall and in the mesentery. The

terminal ileum is most commonly involved, but lesions have been reported in every part of the gastro-intestinal tract.

Joint Symptoms.—Several joints may be affected simultaneously or in succession, especially the knees and ankles. Pain, swelling and tenderness are the characteristic symptoms. The actual lesions resemble those associated with the skin disturbances. Serous exudate or hemorrhage may occur in the joint capsule, synovial membrane and periosteum. Generally no arthritic changes are present, but the local tissue reactions in the joints may produce a chronic osteo-arthritis, such as is seen in hemophilia.

Kidney Symptoms.—The renal manifestations are albuminuria, hematuria and occasionally, a true hemorrhagic nephritis. Renal colic may result from a blood-clot in the kidney pelvis. Generally the condition is benign, and subsides when the other symptoms resolve. On the other hand, a fulminating, acute hemorrhagic nephritis may supervene with fatal issue, or the nephritis may become chronic with subsequent cardiovascular changes.

Hematology.—There is no characteristic hematologic picture for this disease. The number of blood-platelets is usually normal, but it may be increased or slightly reduced. The clot retraction is normal, and bleeding time and coagulation time are within normal limits. The erythrocytes are unchanged. There may be a moderate eosinophilia and occasionally a slight leukocytosis, particularly in the febrile cases.

It should be kept in mind that the classical group of symptoms need not always be present. There may be skin lesions, for instance, without the visceral complications, or any combination of visceral symptoms may occur without the skin lesions. The various names given to this disease indicate the multiplicity of combinations. When purpura was the only lesion, the disease was called purpura simplex. A combination of purpura and urticaria was designated as purpura urticans. Purpura rheumatica (Schoenlein) implied the association of skin lesions and joint symptoms. Purpura abdominalis (Henoch) implied the presence of gastro-intestinal symptoms. The combination of skin lesions, joint symptoms and gastro-intestinal crises is generally known as Schoenlein-Henoch's disease, and perhaps it is advisable to designate this symptom-complex in this man-

ner in order to emphasize the fact that so frequently it forms a definite clinical entity.

Pathogenesis.—An interference with the capillary mechanism, both structural and functional, is the fundamental disturbance which is responsible for the clinical picture. This capillary mechanism may be analyzed into the following components: (1) morphology; (2) tonus; (3) current, pressure and filling phenomena; and (4) permeability. Studies on the nature of the capillaries have been made by many investigators, among whom the work of Lewis, Müller, Krogh and Harrop, and Dale and his associates may be mentioned. What is to be construed under the term capillary is discussed by Lewis.[13] In his opinion, the restriction of the term capillary to the anatomical capillary loop is unwarranted. The capillaries, the minute venules and the terminal arterioles are all simple endothelial tubes. Together they constitute a meshwork which, although from a strictly anatomical standpoint may be divided into three constituent parts, has not been so subdivided physiologically. Agencies which act on the one part, act precisely in the same manner upon the other parts. Müller[14] observed living human capillaries under the capillariscope both in health and in diseased states, and his conclusions are very illuminating. In cases of purpura of this group (Schoenlein-Henoch), he found a picture similar to that seen in the vasoneurotic disorders, and for that reason he included this type of purpura under the vasoneuroses. The capillaries are dilated, lengthened and abnormally shaped. The arterial limb is constricted, whereas the venous limb is dilated.

Krogh and Harrop[15] investigated the differences in permeability for colloidal particles during contraction and dilatation of the capillaries, and found that a solution of the colloidal dye, vital red, will be quantitatively retained in normal capillaries, but will pass through dilated capillaries. This increase in permeability, at least as far as human skin capillaries are concerned, is interpreted by Lewis[16] as being the result, not of simple stretching of the capillary wall, but of an independent change in this wall whereby it becomes unusually pervious. The wall of the skin vessels may be stretched by suction, but simple suction, however intense, never produces the characteristic response. Lewis studied the local vascular reactions in the human skin to various types of stimuli; namely,

mechanical, thermal, electrical, and chemical. In each case the reaction consisted of three components—a primary and local dilatation of the minute vessels, an increased permeability of the vessel wall (the wheal) and a widespread dilatation of the neighboring muscular arterioles. The two former were independent of the nerve supply, while the latter depended on the integrity of the terminal axon branches of the sensory nerve fibers. A precisely similar response was produced by intracutaneous injections of histamine. Lewis postulates that as a result of the injury some substance is liberated in the injured cells, which produces this triple response. He proceeds to draw a series of analogies between histamine and the hypothetical substance, and concludes that this released substance is either histamine, or a substance having a histamine-like action.

Histamine, beta-imidazolylethylamine, is formed by decarboxylation of histidin, which according to Wells[17] is present in every complete protein. According to Abel and Kubota[18] it is produced not only by bacterial decarboxylation of histidin, but also by simple hydrolysis, and is a widely distributed constituent of all animal tissues. Koessler and Hanke[19] state that the human colon contains a large amount of histamine, and explain the freedom from illness of the normal individual by assuming that histamine is rendered pharmacologically inert in its passage through the intestinal wall. Barger and Dale[20] extracted histamine from the mucous membrane of the gut, and Best, Dale, Dudley and Thorpe[21] isolated it from the liver and lung. According to Thorpe,[22] histamine is also found in such organs as striated muscle, spleen, parotid, kidney, pancreas, testis, thyroid and suprarenal. Dale[23] believes that histamine is present as such in the cell interior, being prevented from leaving it so long as the cell membrane is physiologically intact and that it produces its action only if some stimulus or injury causes its escape into the extracellular fluids.

Furthermore, histamine produces symptoms closely resembling typical experimental anaphylaxis. Dale and Laidlaw,[24] studying the poisonous effects of histamine on the capillary mechanism, gave a cat an intravenous injection of histamine and produced a condition presenting numerous points of resemblance to traumatic and anaphylactic shock. The striking feature was a marked loss in blood volume, partly due to stasis and accumulation of blood in the dilated

peripheral capillaries, and partly due to the escape of plasma out of the capillaries. They concluded that an intensification of the action which relaxes the normal capillary tone renders the endothelium abnormally permeable so that it no longer retains the plasma. Likewise, they found that histamine kills guinea pigs by bronchiolar constriction, and rabbits by obstruction of the pulmonary circulation. In these respects, it is evident that the action of histamine is similar to the anaphylactic syndrome produced in these animals by giving them a second injection of an antigen to which they were previously sensitized.

In accordance with these findings, Dale[25] believes that anaphylactic shock is the result of a cellular injury due to antigen-antibody reaction within the cell—a process in which histamine is released. The symptoms of anaphylactic shock in any one species, therefore, resemble the syndrome produced by histamine itself in that species. This same principle Dale believes is also valid in all cases of allergy or hypersensitiveness in which no antigen-antibody reaction is demonstrable, because they all involve a condition of the cells in which a normally harmless substance becomes specifically injurious. The reaction to such injury manifests itself in symptoms similar to those produced by histamine because histamine is actually released by the injury.

Before leaving the subject of histamine, however, it is necessary to point out that the entire case for histamine is built on experimental analogies and inductive reasoning. Histamine has not been recovered from the tissues following injury, and attempts to produce the triple response with fluid taken from a wheal resulting from skin irritation have not been conclusive. Moreover, as Karsner points out,[26] histamine does not account in every respect for the various phenomena of anaphylaxis. Histamine produces neither the temperature changes, nor the alteration of blood coagulability, nor the refractory state typical of anaphylaxis.

The similarity between the symptoms associated with the variety of purpura under discussion and the symptoms observed in the various allergic disorders, especially serum sickness, is very striking. Urticaria, angioneurotic edema, erythema, abdominal colic, diarrhea, painful and swollen joints and albuminuria are common to both groups. Purpura is not generally seen in serum sickness, but both

purpura and gastro-intestinal crises have occurred following the administration of horse serum.[27]

That the entire symptom-complex may occur as a manifestation of food allergy, has been demonstrated in two cases reported by Alexander and Eyermann.[28] Their first case is that of a woman, aged thirty-two, who suffered from an attack of purpura, abdominal pain, melena, hemorrhagic nephritis and joint pains. Skin tests with food allergens gave no reactions, but after experimenting with exclusion diets, it was found that milk produced abdominal colic. When milk was excluded from the diet, the symptoms disappeared but the purpura and abdominal pains returned as soon as the dietary restriction was violated. The second case refers to a boy, aged four, whose symptoms included purpura, melena, abdominal pain, and painful and swollen joints. Here also the skin tests were negative, but the exclusion diets revealed egg as the offending agent. On withdrawing egg from the diet, the symptoms disappeared. When the child was again given egg in order to observe the reaction, the joint pains and purpura recurred. The same authors[29] later presented a series of six cases in which similar phenomena were observed. In one case there were positive skin reactions to egg, potato and wheat. The other patients showed negative skin tests, but as a result of dietary manipulation, such foods as milk, egg, wheat, potato, chicken, bean, fish, lamb and plum were incriminated. In every instance, the symptoms, including the purpuric lesions, could be precipitated by introducing the offending foods into the diet. A similar case was reported by Barthelme,[30] who found positive skin reactions to wheat and egg yolk. Deliberate feedings of wheat produced purpuric spots and joint pains, and egg yolk caused purpura and abdominal pain. By abstaining from either, the patient remained entirely free from symptoms. In view of the direct evidence that we may gather from these cases and the clinical and experimental analogies previously cited, the deduction seems warranted that we are dealing here with an allergic phenomenon, and that its primary manifestation is a derangement of the capillary mechanism.

Undoubtedly some of the manifestations of drug idiosyncrasies may also come under this category. Drugs like arsenic, benzol and quinine are known to produce a symptomatic thrombocytopenic purpura; on the other hand, purpura, urticaria, edema, erythema

and abdominal colic are commonly seen in drug hypersensitiveness in the presence of a normal platelet count. The nature of this reaction is still a highly controversial subject.[31] The experiments of Landsteiner[32] add weight to the belief that drug hypersensitiveness depends not only on the chemical in question, but on a combination of that chemical with the body proteins, which combination in turn acts as an antigen and produces the allergic symptoms. Landsteiner demonstrated that artificial antigens could be obtained by making compounds of simple chemical radicals, such as atoxyl, with proteins. Moreover, serum proteins treated in this manner are antigenic when injected into an animal of the same species as that from which the serum came.

Bacterial hypersensitiveness is another important factor that deserves attention. Glanzmann,[33] for instance, maintains that bacterial allergy is the primary cause of the entire syndrome. He recognizes no specific bacterial agent, but believes that the foreign protein introduced in the course of a bacterial infection is instrumental in the production of toxic substances which function as capillary poisons. This brings up the question of the relationship of purpura to sepsis. The petechial and purpuric eruptions that are not uncommonly seen in sepsis have been generally explained as being the result of small bacterial emboli in the capillaries, i.e., minute skin infarcts. This, however, is not universally true. The occurrence of large ecchymotic areas, as well as petechiae, the orthostatic nature of the lesions, the positive reaction to the tourniquet test and the associated bleeding from mucous membranes demonstrate that in sepsis other factors are also involved. In some instances of sepsis a moderate or a marked thrombocytopenia is found, and in those cases the platelet reduction may also contribute to the production of the lesions. Rosenthal[34] reported eleven cases of subacute bacterial endocarditis in which purpura was a symptom. Of these, seven showed a platelet count of 90,000 or below; two, 130,000; one, 160,000; and one, 200,000. In three cases there was also an absence of clot retraction. The fact that purpura occurs in spite of a normal platelet count, or when there is only a moderate reduction, is evidence that the pathogenic factor is not to be found in thrombocytopenia alone.

Frank's[35] hypothesis is that in sepsis, particularly in subacute bacterial endocarditis, the purpuric lesions are elicited as a result of changes in the capillary endothelial cells due to the participation of the capillary endothelium in the general reticulo-endothelial response, that the infection invokes. This new function that the capillary endothelium assumes is accompanied by a change in the colloidal dispersion of the cell contents, because of which an increase in permeability also occurs. For this phenomenon Frank reserves the name of hemorrhagic endotheliosis. Thus to explain purpura in sepsis there are at least four factors that must be mentioned: (1) bacterial hypersensitiveness, (2) embolic phenomena, (3) qualitative or quantitative alterations of the platelets, and (4) hemorrhagic endotheliosis (Frank).

It is evident from the above discussion that there are types of purpura for which a single explanation is insufficient and which in the present state of our knowledge cannot be properly classified. This group, besides sepsis, includes the purpuric lesions that are seen in chronic nephritis and uremia, hypertension associated with arteriosclerosis, rheumatic fever, scurvy, scarlet fever and jaundice. In uremia and chronic nephritis, there may be a moderate platelet reduction, and in scarlet fever a severe thrombocytopenia may ensue; whereas in jaundice, disturbances in blood coagulability due to alterations in the calcium metabolism are present. No matter what other factors are involved, all these cases are also characterized by changes in the blood capillaries. Whether the capillary changes play the primary rôle, and whether a state of hypersensitiveness is also involved in these diseases, are questions that warrant further investigation.

Finally, the condition of the vasomotor system *per se* must be considered. If the underlying pathology is situated in the capillaries, it stands to reason that a labile vasomotor nervous system, such as occurs in the vasoneurotic diatheses, would predispose to the occurrence of the syndrome. As a matter of fact, purpura, urticaria and erythema are not uncommonly seen in the neuroses, psychoneuroses and the various endocrinopathies. Pratt[36] cites cases of purpura occurring periodically either during or in place of the menstrual flow. In his discussion of angioneurotic edema and acute circumscribed edema, Cassirer[37] concludes that at least in some of

the cases, the etiologic agent acts not directly on the peripheral capillary mechanism, but primarily on the sympathetic and central nervous systems. His final conception is that for this entire group a labile sympathetic system is the foundation on which the symptoms are constructed. This author also raises the question as to whether as a result of the primary neurotic and psychoneurotic influences, toxic substances are developed which are able to act as poisons on the peripheral capillary mechanism. Whether or not such substances are really produced and to what extent they resemble or actually are allergens, are interesting matters for speculation. Perhaps here also, as Lewis infers, a release of histamine, or histamine-like substances may be the underlying factor.

Diagnosis.—The character of the skin lesions, the joint pains, the visceral crises and the absence of thrombocytopenia help to establish the diagnosis. Between allergic purpura and the thrombocytopenic variety, it is as a rule not difficult to distinguish. In the latter, there are a marked platelet reduction, an increased bleeding time and a nonretractile clot. The skin lesions are not exudative, and the bleeding from the mucous membranes is generally extensive. The visceral complications are absent. If hematuria occurs, it is not associated with a hemorrhagic nephritis. The capillary lesions demonstrated with the capillariscope in cases of allergic purpura are not found in thrombocytopenic purpura.

Treatment.—The treatment should be directed along lines similar to those employed in other allergic disorders. In mild cases of short duration no special therapy is necessary. Where the symptoms persist for a considerable length of time or where there are numerous relapses, an attempt should be made to determine the presence of a specific allergen by means of the various skin test methods and exclusion diets. If a specific agent is found, it should be eliminated from the diet, or measures directed towards desensitization may be instituted. Non-specific protein therapy with typhoid and colon bacilli, milk, casein, peptone and tuberculin may be tried. Calcium is recommended, either as calcium lactate by mouth or as calcium chlorid for intravenous use. Adrenalin and ephedrin may give temporary symptomatic relief. For the joint pains, the salicylates are employed advantageously. In the presence of hematuria or

nephritis the measures generally observed in the treatment of these conditions, including diet and fluid regulations, are essential.

The gastro-intestinal symptoms deserve special attention. There are numerous case records in the literature of patients belonging to this group who were subjected to laparotomies because of an erroneous diagnosis, such as acute or chronic appendicitis, acute or chronic cholecystitis, intestinal obstruction, intussusception and perforated gastric or duodenal ulcer. This emphasizes the fact that when operative interference is contemplated for any of these conditions, the possibility that the symptoms are merely the visceral manifestations of an allergic episode should be kept in mind and carefully ruled out. On the other hand, the more serious complications, although rare, do occur, and then surgical intervention in order to reduce an intussusception, resect a gangrenous portion of the bowel or establish drainage in peritonitis, becomes imperative, and indeed, a life-saving measure.

Summary and Conclusions.—Purpura is divided into two main groups: (1) purpura due to a reduction in blood-platelets (thrombocytopenic purpura); and (2) purpura due to changes in the blood-capillaries.

Allergic purpura is characterized primarily by morphologic and functional changes in the capillary mechanism resulting in abnormalities in the structure of the capillaries, in current pressure and filling abnormalities, and variations in the permeability of the capillary endothelium. It is not essentially a hemorrhagic disease and has no characteristic blood findings.

Numerous etiological agents are involved. Instances are on record where the disease has followed the administration of horse serum or where a definite food allergen is responsible. Drug hypersensitiveness, bacterial allergy, vasoneurotic and endocrine disturbances and histamine are discussed as etiological factors.

The treatment follows the therapeutic measures generally employed in all allergic diseases; *e.g.*, elimination of the cause where that is possible, desensitization to a specific allergen, non-specific protein therapy, and symptomatic relief as indicated. For the severe gastro-intestinal complications, surgical intervention may be required; for the renal complications, the well-known measures employed in the treatment of nephritis are indicated.

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Diagnosis and Treatment

THE DIFFERENTIAL DIAGNOSIS OF PEPTIC ULCER*

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Not so long ago, clinicians were almost universally of the opinion that peptic ulcer was a rather remarkable phenomenon among diseases in that its pathogenesis was seemingly doomed to perpetual anchorage in a sea of obscurity. Recently, however, a tendency to regard the problem as not wholly impossible of solution has manifested itself.[1] The many theories of the origin of peptic ulcer seem to be undergoing a gradual evolution into an ordered, albeit still intricate, pattern. However, this order-out-of-chaos materialization is still far from complete and so medical science continues to regard extant data concerning the etiology and pathogenesis of peptic ulcer as insufficient for a basis of treatment. Treatment, instead of depending upon etiology, must therefore rest to a very large degree upon existing pathology. This being the fact, it is absolutely essential to be certain that peptic ulcer exists before treatment for it is instituted.

Many intra-abdominal affections, and some extra-abdominal affections, give rise to symptoms so closely simulating those of peptic ulcer that often differential diagnosis is far from easy. Occasionally, it is wholly impossible. Obviously, if a patient without peptic ulcer is treated for such a condition, or if one with pathology elsewhere in the body is treated for peptic ulcer and not the actual lesion, the results must be disappointing. For this reason, it is not an idle expenditure of energy for the one who has at heart the successful

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treatment of his cases to pause from time to time to take an inventory of the differential data in his diagnostic armamentarium. During this process, he re-summons to his finger-tips the knowledge he acquired in his student and postgraduate days, and adds to the total the findings of subsequent experience.

It is because we believe that the personal interchange of the results of experience is of the utmost practical value in the progress of any science, but particularly of medicine, that we venture to present below certain observations concerning the differential diagnosis of peptic ulcer from diseases with symptoms simulating those of peptic ulcer which have emerged from our own retrospective study and summation.

In this recapitulation, we have come to realize that the following diseases, giving rise to symptoms like those of peptic ulcer, are, in our experience, the most common:

   I. Functional gastric hyperacidity with or without gastric
        catarrh
  II. Chronic appendicitis
 III. Chronic gall-bladder disease
 IV. Epigastric hernia
  V. Colica mucosa
 VI. Calcified mesenteric glands
VII. Bothriocephalis latus
VIII. Angina pectoris
 IX. Tabes dorsalis
  X. Duodenal irritation.

I.   FUNCTIONAL HYPERACIDITY WITH OR WITHOUT GASTRIC CATARRH

With the advent of increasingly exact methods of diagnosis during the last twenty years, there has been a tendency to look lightly upon functional disturbance and to consider that for every functional disturbance there must be an organic basis. The discussion of such a subject as the differential diagnosis of functional hyperacidity and peptic ulcer may, therefore, appear antiquated. However, when one regards the subject with real clinical critique, it becomes evident that the conception that there must always be an organic basis for a functional disturbance is exaggerated.

Every organ in the body can, under certain conditions, give rise to functional disturbance with symptoms closely simulating those of organic disease, without any pathologic basis. We cannot agree with von Bergmann[2] that the so-called "neurosis of organs" has ceased to exist, and that careful search in every case would reveal an organic basis. Von Bergmann bases his claim on the fact that, in most cases where a functional disorder is diagnosed, one can, by careful examination, actually detect some objective finding. Do transient objective findings, however, whether laboratory, roentgenologic or palpatory and no matter how outspoken, denote absolutely that existing symptoms are due to underlying pathology? Experience dictates a negative answer. Many an abnormal laboratory finding—even transient icterus, roentgenologic evidence of deformity of the viscera or an occasional transitory palpatory finding of tumor—has proved to be due to purely functional disturbance of the organ in question. It is well known that in gastric disturbances of a secretory nature one encounters high acid figures alternating with low acid figures (heterochylia Hemmeter) and it is known that marked motility disturbance characterized by delay in emptying or by hastened emptying of the stomach, with spasm of different parts of the organ simulating organic disease, may exist without an organic basis.

Naturally, it is often very difficult to differentiate as to whether an organic disease is present or the disturbance under analysis one that is purely functional. It is self-understood that occasionally a neurotic individual is afflicted with an organic disease with the neurotic symptoms so pronounced that the organic lesion is masked and perhaps overlooked. Many patients have suffered the consequence and we the disgrace of such mistakes. Some physicians, in order to protect themselves from criticism, hasten to the extreme of telling the patient that there is something organically wrong, and go so far, even, as to treat him on that basis when truly that is not the case. Unhappily, many of these patients become introspective. A great many, indeed, become confirmed hypochondriacs. And the damage does not inhere solely in the psychic effect on the patient. We may seriously undermine the natural function of the patient's organs by such unmerited treatment. To illustrate, if a case of gastric functional disturbance is treated on the basis of ulcer, the

effect is much as when a healthy limb is unnecessarily immobilized for a number of days. Some time must elapse after removal of the plaster before the limb is able to resume its normal function owing to the period of disuse.

The correct interpretation of neurotic symptoms and the proper guidance of patients so afflicted is within the domain of clinical intuition rather than in that of objective examination. Fortunately, however, there are a number of criteria to guide us.

History.—The very act of taking a patient's history can assist us to judge whether or not a case is functional, if we note the manner in which a patient describes his symptoms.

There are two types of persons, the rather common type who greatly exaggerates and the rarer one who minimizes all symptoms. The former is anxious to attract sympathy and to have his physician believe him organically ill. The latter wishes the physician to believe him sick but is filled with fear lest he be told he has an organic disease. The former describes his symptoms in elaborate detail and in superlative terms, with a simile for each symptom. He states that his pain is as sharp as lightning or that it sticks like needles or that it cuts him like a knife. He points with his finger to the seat of symptoms, very often to an exact point in the epigastric region with no hint of radiation, or if any only a very slight one. His pain is such that the merest touch of his clothes against his skin annoys him; on the other hand, deep pressure affords relief. Through contact with sick people he may have learned that ulcer is accompanied by hunger pain. If so, he dwells on this symptom in the hope that his physician will give credence to his complaints. Whether this is volitional or due to his susceptibility to suggestion cannot be judged. The patient who minimizes—although his neurotic symptoms may be accompanied by an organic disease and although he may actually suffer hunger pain relieved by alkalis—will voluntarily withhold such information and will deliberately evade giving answers to direct questions. He is the much more difficult of the two to diagnose. Although he is markedly introspective with a digestion that is easily disturbed, readily admitting that his symptoms depend on the kind of food he takes, he minimizes the severity of his symptoms lest, otherwise, he be told he has an organic basis. His reticence sometimes actually masks an organic disease. One of the

reasons the psychoanalyst succeeds so well with many of these cases is his minute attention to all the details mentioned by the patient and his ability to elicit information the patient desires to keep to himself. Careful attention and an analysis of symptoms are necessary when we deal with the neurotic individual. The very impression we make upon him may be of therapeutic aid.

When the symptoms are purely neurotic in origin, they are exaggerated as a result of the slightest physical overwork or indiscretions in diet. This is not so with the symptoms of uncomplicated peptic ulcer. During remissions the ulcer patient boasts of being able to eat most foods with impunity. Overwork and psychical trauma rarely cause a relapse. The relapse is generally directly dependent on seasonal changes and is quite often preceded by a mild infection. The neurotic individual, however, is practically never free of symptoms and feels he must always be careful. Often he cannot be induced to eat despite the fact that his gastric functions would tolerate and even be benefited by food. This is one of his phobias. The ulcer individual, on the contrary, is neglectful largely because he knows that during the free interval no matter how indigestible the food it is tolerated by his digestive tract. It is only during the period of his active symptoms that a dietetic régime can be enforced. Many cases of uncomplicated peptic ulcer very quickly respond to dietetic treatment and often disappear without any treatment, but the symptoms of functional origin rarely yield to treatment or, if so, only transiently.

The person with functional hyperacidity, as a rule, has stigmata of neurosis or neurotic symptoms in varying degree referable to organs other than the gastro-intestinal tract. At one time his secretory symptoms will be more pronounced, at another time the sensory symptoms will prevail. Irrespective of the system in which the symptoms temporarily predominate, however, sensory manifestations are always in the foreground. The secretory symptoms are characterized by sour regurgitations. The patient feels that his stomach is full and will not empty. He belches continuously in order to rid himself of excessive gas but this gives him at most only temporary relief. His belching differs from that of the peptic ulcer individual because the latter can induce belching by taking bicarbonate of soda and is greatly relieved thereby, because the tension in his stomach

is actually lessened. The neurotic individual gains no relief because he is an air-swallower. With each belch more air is swallowed and tension, instead of diminishing, increases.

Status.—In the majority of cases, the status of the individual is indicative. The young person who has neurotic gastric symptoms is generally asthenic in type. The majority of the older persons with these symptoms are of the hypersthenic type. The reason the young, asthenic individual develops such symptoms is because his organs have not grown to the tasks of life and are not readily accommodating themselves. The cause, in the hypersthenic individual, is most likely beginning intra-abdominal vascular changes. In the female the menopause with its accompanying galaxy of neurotic behavior symptoms may bring about symptoms simulating ulcer. It has been our experience that the asthenic youth with gastric ulcer has other outspoken stigmata of vagotonia, and that the plethoric, older individual with gastric ulcer symptoms has noticeable stigmata of sympathicatonia. Vagotonia is frequently enough associated with purely functional gastric disturbances to be in itself of clinical importance. It may mark a preulcerative state or, as long ago emphasized by von Bergmann, may be the actual cause and continuous accompaniment of peptic ulcer.

Objective Findings.—The objective examination of a neurotic patient is more important than that of one in whom the symptoms point positively to ulcer. The purpose is twofold: (1) to rule out the presence of an organic lesion, and (2) to study the individual so carefully as to convince him the examination was complete and that no organic lesion could have been overlooked. If we can prove to him that his symptoms are not due to an organic lesion, this in itself may serve as a therapeutic agent. At times, it may be necessary to tell the patient that we are convinced that no ulcer is present but that a small erosion exists which, if treated, will heal within a short time. These occasions are rare but when the patient is one who requires such handling the effect may be doubly beneficial. If a small ulcer or erosions actually exist or if a preulcerative state is present, the treatment will have both healing and psychical value.

Many neurotic persons have manifestations of imbalance in the vegetative nervous system, such as the young patient with cold, wet hands who perspires readily all over his body, particularly in the

axilla. The young individual—and sometimes the one over fifty—may have a tendency to sinus arrhythmia, depending upon whether vagus or sympathicus symptoms predominate. There is a marked alteration of pulse rate. With the vagus predominating, there is usually a slow pulse or it is considerably slowed by the exercise of slight pressure on the eyeballs (Aschner phenomenon) or when the patient is made to bend forward (Goldscheider sign). There is marked dermographica, indiciating a sensitive vasomotor apparatus.

Secretory Phenomena.—In most cases there is a decided variation in the quantity of gastric secretion and in the acid figures. At one examination there may be a very high acidity and at the next very low.

Motor Function.—This may be so disturbed, transiently, as to simulate disease. Marked hyperperistalsis and extremely rapid emptying may be present. Or delay in emptying, without evidence of atony, may be noted, sometimes without any evidence of disturbed peristalsis. The motor function of the colon is likewise disturbed. Constipation of a spastic nature is the rule. Once in a while we encounter cases where constipation alternates with diarrhea and, more rarely, cases of diarrhea alone consisting of a few watery stools in the course of the day unaccompanied by tenesmus and without blood but with slight quantities of mucus unmixed with the stool.

Roentgenologic Examination.—This, instead of clarifying, may confuse. Regional, local or even generalized spasm of the stomach may bring about such deformity as to simulate ulcer and even cancer of the stomach. Persistent spasm of the first portion of the duodenum may be so outspoken as to give rise to a phthisis bulbi. These spastic manifestations give rise to symptoms that are so severe that often a patient is willing in his search for relief to submit to laparotomy—and sometimes to more than one. At operation, however, even the most careful surgeon finds himself unable to explain the patient's symptoms because, under anesthesia, the spasm of the stomach is relieved. At most there is only a very thickened pylorus, the result of moderate hypertrophy.

These spastic phenomena of the stomach or duodenum may be present at a fluoroscopic examination and disappear spontaneously within a few minutes. At other times, the spasticity does not disappear until large doses of belladonna are administered over a

period of several days, as advocated by Carman,[3] and sometimes not until after the administration of belladonna with papaverin as advocated by Holzknecht and Luger.[4]

Association of Functional Hyperacidity with Catarrh.—It is important to emphasize that very often what we call functional hyperacidity is associated with, or is caused by, gastric catarrh. In view of the fact, however, that the study of the stomach at post-mortem cannot determine the presence of catarrh unless it is very severe—like that following cirrhosis of the liver—the pathologists for a while rather ridiculed the clinical diagnosis of catarrh. Such a diagnosis practically disappeared until Konjetzny[5] again took up the study of gastric catarrh with great care and found it present in practically all cases of gastric ulcer and for that reason attributed gastric ulcer to gastric catarrh. Since then, the study of catarrh has been more widely carried on and this diagnosis is now rather too frequent. Konjetzny has, however, made us aware of the fact that gastritis hyperacida, as Strauss[6] calls it, may occur. The diagnosis, however, must be based not upon symptoms alone but upon objective findings. It has long been known that the finding of excess mucus or even microscopic evidence of mucus and a large number of leukocytes is an indication of catarrh. Strauss advocates a method to determine catarrh which we feel ought to gain ground. He gives the patient eight, ten, or sixteen ounces of tea which serves as a color medium and half an hour later aspirates the gastric contents, filtering a definite amount, fifteen or twenty cubic centimeters. Normally, the contents pass through the filter in fifteen or sixteen minutes. The prolongation of this period depends on the quantity of mucus—the more mucus the longer the time required for filtration. The filtrate is stained with methylene blue. If it takes the stain deeply, this indicates that the mucus does not come from the stomach but from the pharynx or nose. If it does not stain at all or only lightly, it comes from the stomach. If the microscopic findings show a large amount of mucus, particularly a great many leukocytes, one may definitely state that there is gastric catarrh. It is most essential from the diagnostic and therapeutic standpoints to determine whether we are dealing with an ordinary functional hyperacidity or hyperacidity plus catarrh.

II. CHRONIC APPENDICITIS

It is well known that chronic appendicitis may simulate peptic ulcer in every detail even to the extent of gastric hemorrhage, although why it should cause profuse gastric hemorrhage cannot be explained. It is possible that it causes a disturbance in the gastric capillaries so that diapedesis results, giving rise to diffuse bleeding (typus-Dieulafoy). This capillary diapedesis may be the result of the deleterious effect of toxins on the capillaries. The gastric hemorrhage that arises from chronic appendicitis is refractory to medical treatment. Should it yield, it is only for a short time. Blood transfusions and other measures have but slight effect upon the anemia. There are three other extragastric affections that give rise to gastric hemorrhage but these are readily recognized as a rule. They are, cirrhosis of the liver, thrombosis of the splenic vein with Banti's symptom complex, and thrombosis of aneurysm of the hepatic artery. In the absence of these and in the presence of a profuse gastric hemorrhage that cannot be influenced by medical treatment, one must think of chronic appendicitis as the causative factor.

Many important internists and surgeons are unwilling to agree that chronic appendicitis is a cause of symptoms resembling those of gastric ulcer. They claim that such symptoms continue in many individuals even after the removal of a diseased appendix. However, gastric catarrh, needing care after the appendectomy, may have been the cause of the chronic appendicitis. Again, disturbed motor and secretory gastric functions may persist after the appendectomy and require postoperative attention. If not given, the unabated gastric irritation may eventually lead to the formation of an ulcer. Extensive pericecal adhesions or adhesions extending to the right hypochondrium may exist after appendectomy and cause the gastric symptoms, or the appendicular stump itself may cause irritation in the ileocecal region and, occasionally, typhlitis and displacement of the caecum, or a thick caecum, may hinder the function of the colon —especially the ascending colon and the junction of the caecum and ileocecal region—so that gastric symptoms continue after the diseased appendix has been removed.

Another contention that a chronically diseased appendix is *not a* cause of gastric ulcer symptoms is that often such a diseased ap-

pendix is removed with no ulcer present at the time of operation. Yet, months or years later, following a period when the patient continued to have his peptic ulcer symptoms, another operation is performed and a large ulcer found. The opponents to the theory of the diseased appendix as the cause of the ulcer symptoms claim that the existence of the ulcer was overlooked during the first operation. Perhaps a small ulcer, impossible of detection by the surgeon, was present, and medical treatment after the appendectomy might have prevented the development of the large ulcer. We know of three cases, in our own experience, however, where a small peptic ulcer was noted by the surgeon at operation, in association with a chronically diseased appendix, but as there was no reason to believe it had occasioned mechanical disturbance sufficient to warrant gastric surgery, this was not performed. Only the diseased appendix was removed. Although many years have since passed, the patients have had no return of their ulcer symptoms.

Sir Humphry Rolleston has divided the symptoms of chronic appendicitis into four groups; namely, mechanical, toxic, infectious and reflex. It is the fourth group, where the symptoms are reflexly referred to the stomach, that engages our attention here.

History.—Although the history of an acute attack is of paramount importance, one encounters many cases where for one reason or another such a history cannot be obtained. Possibly the attack was too mild to attract a proper diagnosis or it may have happened during the early years of the patient's life and may have been attributed to intestinal indigestion. It is often worth while to watch the patient while he describes his symptoms. He talks about pain in the stomach and points to the appendix.

The patient with chronic appendicitis and gastric ulcer symptoms is not entirely free of symptoms during any period of remission, contrasting in this respect to the peptic ulcer patient who is symptom-free for months at a time. He responds with abnormal sensations to all irritation, particularly to dietary indiscretions. Constipation is especially troublesome to him.

Secretory disturbances such as marked pyrosis and sour regurgitations may exist, the pyrosis being present most of the day and unaffected by bicarbonate of soda, or at least not as affected as the pyrosis of peptic ulcer. It does not disturb his sleep. There may be

periods when sensory symptoms predominate and other when the hypersecretory symptoms are more outspoken. Motor disturbances appear as marked functional disturbances in the epigastric region and occasionally as delayed emptying of the stomach causing the patient to vomit food eaten ten or twelve hours before. When the sensory symptoms predominate, the patient complains of actual pain an hour or two after meals. It is in the epigastric region but is never as severe as in true peptic ulcer except when marked pyloro-spasm occurs intermittently and produces the acute attack that resembles perforated peptic ulcer.

Objective Examination.—1. *Pressure Tenderness.*—The ileocecal region is sensitive to pressure even in normal individuals and so its diagnostic import must be judged wisely. If the appendix is the cause of the gastric symptoms, the patient will usually complain of pain in the epigastric region when pressure is exerted over it. MacKenzie[7] explains this local tenderness by stating that it results from spinal nerve irritation of the tenth and twelfth dorsal segments of the cord and we believe that this is a responsible factor, and moreover, that if this irritation continues to the point of a summation of irritating impulses, then constant pain in the organ supplied by the segment will occur and it may not be relieved by the removal of the diseased organ.

2. *Hyperesthesia.*—This is present in many cases where the appendix is the cause of gastric symptoms. It may originate in that part of the segment of the cord from which the spinal nerves emerge supplying the skin overlying the organ. An impulse from the affected organ to the segment of the cord travels from this to the brain and from there efferently to the skin. The process is one of double efferent impulse.

3. *Hyperesthesia and hyperalgesia*, when present with a diseased appendix, are usually confined to a space over the right side of the abdomen known as Sherren's triangle. According to Fraser[8] they are found in 50 per cent. of the cases, although present only when the appendix is overdistended and filled with inflammatory exudate, parasites or concretions.

4. *Livingstone's Phenomenon.*—Livingstone[9] has found that any traction of the skin over the ileocecal region—the skin being pulled upward and outward by the thumb and index finger—gives a

distinct sensation of pain. This sign is not present in all cases, but when found points strongly to a diseased appendix.

5. *Pain in the Right Loin.*—In some cases an area of hyperesthesia over the right loin is distinctly typical. When an appendix is retrocecally located, there may be referred pain in the right loin simulating renal colic, differing from it only in that it is more or less continuous and often associated with digestive disturbances.

6. *Abdominal Reflexes.*—If the abdomen is not pendulous and there is no marked obesity, whenever hyperesthesia is present there is also a marked increase of the abdominal reflexes on the affected side. This is important, inasmuch as it indicates that the hyperesthesia is not due to underlying peritoneal irritation, which would cause rigidity of the overlying abdominal wall, but is caused by viscous irritation. Klein [10] differentiates hyperesthesia obtained when the skin is pinched over a diseased organ from the contraction reflex that is the response to a scratching of the skin over a particular area. He found that when the peritoneum is affected, the contraction reflex is absent.

7. *Percussion Tenderness (Mendel's sign).*—Although some authors find this a frequent sign in chronic appendicitis we have encountered it much more frequently over the duodenal region when there is a duodenal ulcer.

8. *Tenderness on Pressure Over Left Shoulder Clavicular Joint.* —We have found in chronic appendicitis, giving rise to marked gastric symptoms, considerable tenderness when pressure is exercised over the anterior part of the left border of the shoulder clavicular joint near the acromium process, corresponding to a sensitive pressure point on the right side in case of gall-bladder disease.

9. *Pain on Inflation of Colon (Bastedo's sign).*—When the colon is inflated with air the patient experiences pain or discomfort over the appendicular region if the appendix is diseased, or if it is distended with water the patient experiences pain over the appendicular region at the time of distention.

10. *Pain Upon Rectal Examination (Reder's sign).*—The patient will sometimes state that he feels pain in the appendicular region when he is examined rectally.

11. *Pain on Pressure Over Left Side of Abdomen (Rovsing's sign).*—Pain is experienced in the appendicular region if pressure

is exercised on the left side of the abdomen at a point corresponding to McBurney's point on the right side.

Secretory Findings.—In a large percentage of cases, although there may be symptoms of hyperacidity and hypersecretion, the acidity figures are normal and actual hypersecretion is absent. In some cases, however, when the acidity is disturbed, there is a manifestation of hyperacidity. The acidity may be higher than in gastric ulcer, but it is never as high as when hyperacidity is present in duodenal ulcer. Pyrosis and sour regurgitations, in peptic ulcer, usually correspond to actual hyperacidity. One finds, by means of the fractional determination of gastric acidity, that in chronic appendicitis the hyperacidity, when present, is not continuous as in duodenal ulcer. After an hour and a half or two hours the acid figures are those of a normal person or but slightly elevated. Fenwick[11] has sought to differentiate chronic appendicitis on the basis of gastric secretions by claiming that if the mucous membrane of the appendix is the sea of chronic ulceration there is usually hyperacidity. If the chronic appendicitis is complicated by pericecal or appendicular adhesions, subacidity is present.

X-ray Examination.—The most important diagnostic means is the roentgen examination. This makes it possible for us to visualize the appendix and judge its influence, when diseased, upon adjacent organs. No special effort is, as a rule, needed to fill the appendix. It is generally visualized after six, eight or twenty-four hours. Czepa[12] recommends the following method for filling an appendix that will not fill otherwise. Czepa gives epsom salt after the barium meal. Three, six or eight hours later, he examines the ileocecal region fluoroscopically and roentgenographically. If the appendix does not fill under fluoroscopic control, he exerts pressure over the ileocecal region and so succeeds in filling it. The mere failure of an appendix to fill, however, or the fact that it fills and remains filled a longer time than normal, does not justify a conclusion that the appendix is diseased.

1. *Size.*—This generally depends upon the status of the individual. If its length is strikingly abnormal (Fig. 1), and out of proportion to the remainder of the abdominal viscera, it is presumable that its size is due to hypertrophy resulting from disease. An exceptionally small appendix must be considered pathologic, the

FIG. 1.

Long appendix.
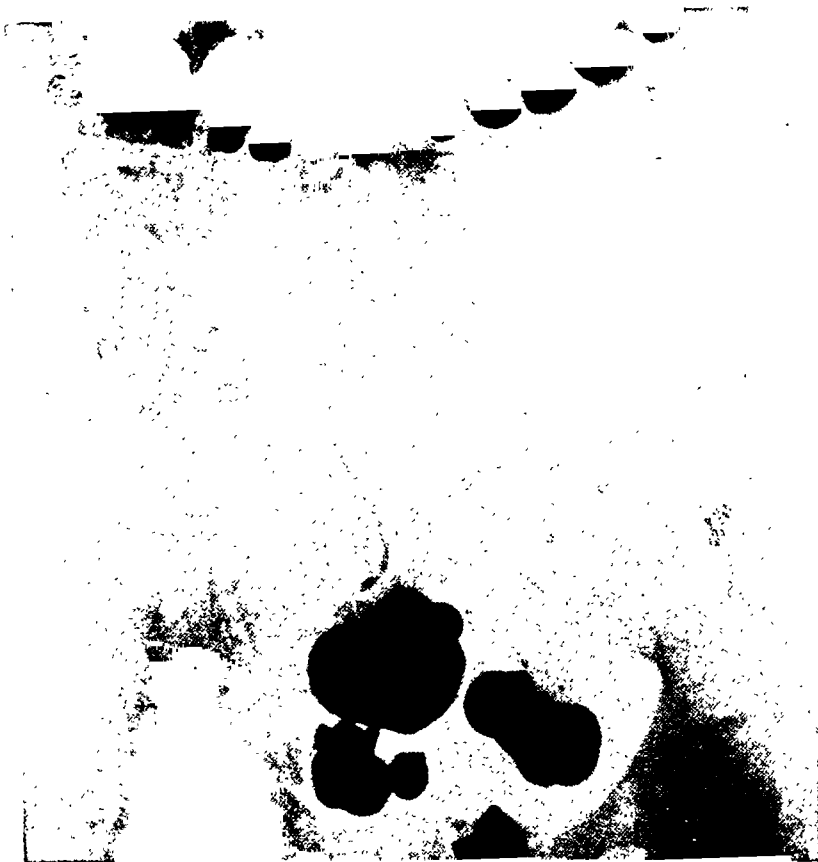
Fig. 3.

Malposition of appendix.

Fig. 2.

Circular appendix.

small size being due to the fact that the greater part of the appendix is obliterated by chronic inflammation. In such cases the surgeon generally finds an abnormally long appendix, despite the fact that it was very small on the roentgenogram.

2. *Shape.*—Usually the base of the appendix is much wider than the apex. If the reverse is true, that is, if the middle portion is wider than the base, this is generally evidence of appendicular inflammation. Sometimes during the examination the entire appendix will lie in a circle (Fig. 2) or in the shape of an "S" or in some other odd figure. If such distortion persists throughout an examination, the appendix is probably pathologic.

3. *"Contractions."*—Max Cohn [13] is convinced that visualized "contractions" are but indications that the appendix has segmentations and empties like the colon. The "beaded" appendix, according to Cohn, is an indication of the normal physiology of the appendix.

4. *Motility.*—If an appendix is persistently filled for days, maintaining a continuous shape, it is generally diseased.

5. *Mobility.*—Where the caecum is normally movable, the appendix is expected to be equally mobile. If the appendicular mobility is restricted, although the caecum is freely movable, the lack of mobility of the appendix is probably due to appendicular adhesions. In the hypersthenic individual, the caecum is nearly always high, with a short mesentery, the mobility being limited and not demonstrable in even a normal state.

6. *Position.*—The position of the appendix varies greatly. It may be located very low in the pelvis, behind the caecum, or it may point to the left side of the abdomen. The pathologic significance of its position can be judged only if its relation to the ileum is considered. Situated very low in an asthenic individual, the rest of whose abdominal viscera are low, it is merely part of the general status. Situated low and pulling down the ileum in one whose caecum and the remainder of the colon, particularly the hepatic flexure, are in a normal position, it is quite likely abnormally situated, due to adhesions. This is especially true if the appendix is low and the ileal coils are high, particularly if the latter lie in the median or to the left of the median line. Should the ileal coils be dilated and contain gas, a diagnosis of ileocecal adhesions, the result usually of chronic appendicitis, may be made with certainty.

The close adherence of the appendix to the caecum usually causes adhesions between the diseased appendix and the caecum so that the abnormal position is present in both conditions. With the appendix retrocecally situated, pathologically, the caecum is generally very high. If the appendix is pathologically low in the pelvis or is pulled to the left side of the abdomen, the caecum is correspondingly displaced (Figs. 3, 4 and 5). But, it must be emphasized, the position of the caecum is to be considered abnormal only if its position does not correspond to the status of the individual. In *caecum mobile* both the appendix and the caecum may be found in, an abnormal position—either very low or to the left of the median line—without underlying pathology.

7. *Effect on Adjacent Organs.*—Marked cecal spasm and particularly ileocecal stasis are signs of appendicular disease. These may be so marked as to simulate the Stierlin complex of ileocecal tuberculosis. (Fig. 6.) Again, marked dilatation of the caecum may be present.

Of less diagnostic importance, but worthy of consideration, is the putty-like appearance of the caecum persisting for days after the colon is empty. This shows a co-affection of the caecum, probably due to catarrh of the mucous membrane of the caecum (typhlitis or peri-typhlitis secondary to chronic appendicitis).

8. *Tenderness Over the Appendix, Fluoroscopically observed.*— Such a finding is of value only if one is sure the tenderness is localized over the entire appendix and only when it varies with the position of the organ. Sometimes dilated ileal coils holding the contrast meal much beyond the normal time may be the result of spasm of the ileocecal sphincter, as pointed out by Case.[14]

9. *Ileo-cecal Valve Incompetency.*—Inasmuch as this is encountered in many ulcer individuals its pathologic significance can be utilized only in association with other signs of chronic appendicitis. Where there is marked ileocecal valve incompetency, a diagnosis of disturbance in the ileocecal valve is justifiable, due generally to a diseased appendix with ileocecal adhesions.

10. *Partial or Localized Spasm of the Stomach.*—This is one of the indirect signs serving to explain gastric symptoms arising from chronic appendicitis. Localized spasm, as seen as an indentation on the greater curvature in the pars media, is best demonstrated

FIG. 4.

High caecum, low appendix.

FIG. 5.

Left-sided appendix.

FIG. 7.

Gall-bladder visualized with patient in left latero-anterior position.

FIG. 6.

Contracted caecum due to adhesions simulating Stierlin complex.

when, under the fluoroscope, pressure is exerted over the appendicular region. In our experience, this spastic indentation persists only a few minutes, differing from spastic indentation due to intrinsic disease of the stomach proper.

Partial gastrospasm, occasionally encountered, may be so marked and persistent as to simulate the pivot-shaped pylorus due to cancer. It is most often encountered in the vagotonic individual.

Spasm of the sphincter pylori to the extent of giving rise to marked delay in emptying of the stomach is uncommon in chronic appendicitis. When it does occur it is generally at the time that the chronic appendicitis is giving rise to active ulcer symptoms. Despite the normal position and the outline of the stomach and duodenum, we encountered gastric residues often beyond eight hours, due, probably, to actual spasm of the sphincter pylori. This spasm is noted in the fact that the pylorus is unusually dilated and is so large that whatever contrast food leaves the stomach does so in the form of a very narrow stream. Fluoroscopically, such spasm differs from stenosed pyloric obstruction in that the excessive peristaltic waves characteristic of pyloric stenosis are absent.

11. *Spasm in the Small Intestines.*—Chronic appendicitis with marked gastric symptoms may also give rise to spasm in the small intestines, especially the entire ileum, and often in the sigmoid.

12. *Dilated First Portion of the Duodenum.*—A not infrequent indirect roentgen sign in chronic appendicitis is a markedly dilated first portion of the duodenum.

III. GALL-BLADDER DISEASE

It is a remarkable fact that clinically chronic gall-bladder affection more often simulates duodenal ulcer than gastric ulcer. In the rare cases where it simulates gastric ulcer, the symptoms are those of an ulcer situated very high in the stomach with accompanying signs of cardiospasm. We have encountered three cases where a definite history and clinical evidence of gall-stones existed with symptoms of periodic attacks of cardiospasm. In one case, the cardiospasm was persistent. The other two patients were entirely relieved of their peptic ulcer symptoms, including cardiospasm, by cholecystectomy.

A stone-containing gall-bladder less often simulates duodenal

ulcer than the chronically inflamed gall-gladder or gall-bladder or biliary duct dysfunction without marked pathologic changes (cholecystopathie). Dyskinesia (Westphal) is due in the majority of cases to disturbed function of the sphincter of Oddi and of the gall-bladder without any demonstrable pathology. This sphincter fails to relax and the gall-bladder cannot empty despite the fact that its activity is excessive. When a gall-bladder is hypertonic and there is excessive activity, the condition is *dyskinesia cholecystopathie hypertonica.* When the sphincteric action is normal but the gall-bladder is markedly atonic and cannot empty, the condition is called dyskinesia cholecystopathie atonica. In either condition, stagnation of the bile in the gall-bladder gives rise to clinical symptoms. Where the sphincter spasm plays the greater rôle the colic may be very severe despite the absence of calculi. Such colic is not relieved by morphin but may be relieved by atropin. For the atonic gall-bladder the best drug is pituitrin, which stimulates gall-bladder contractions and rids the organ of its contents.

The biliary colic in dyskinesia is due to an imbalance in the action of the vegetative nerves supplying the biliary ducts. It is not surprising that such imbalance may also exist in the adjacent organ; namely, the duodenum, and give rise to duodenal ulcer symptoms. The symptoms, whether biliary or duodenal or both combined are usually more persistent than those due to actual organic disease of the biliary ducts or duodenum, and often do not yield to medical treatment, thus eventually necessitating surgical intervention. Generally, to the great surprise of the surgeon, the pathologist fails to find any changes in the removed organ and becomes justly critical. Still, when one follows these cases clinically, he finds that often they are symptomatically relieved by the removal of the gall-bladder.

At times the duodenal ulcer symptoms are caused by direct adhesions between the duodenum and the gall-bladder. Again, they are due, undoubtedly, to associated catarrh of the duodenal mucosa. Very rarely, they are caused by what Barclay has termed duodenal irritation.

Whatever the cause of the ulcer symptoms arising from a gall-bladder affection, differential diagnosis is generally impossible from the clinical symptoms alone. Reliance rests mainly in a very careful

objective examination, which, with the present methods at hand, leads to a proper diagnosis in a high percentage of cases.

History.—The history of an attack or attacks may date so far back as not to be recalled spontaneously by the patient. Such a history—even though elicited—is particularly valuable in women who date their attack to pregnancy, parturition, or to the nursing period. It has been our experience—and this is worthy of emphasis —that if a man of feminine characteristics is afflicted with peptic ulcer symptoms, these are due more often to gall-bladder affection than to peptic ulcer. In these individuals the increase in the cholesterol content of the blood is a great aid in tracing the symptoms to their proper origin.

In the absence of history of an acute attack, if there are no absolutely free intervals—that is, if, most of the time, the digestive tract is extraordinarily sensitive, and especially if the patient is sensitive to fat—one may think away from peptic ulcer, and lean strongly to a diagnosis of gall-bladder disease. In uncomplicated peptic ulcer, during the free interval, the majority of patients can partake of almost any food without discomfort.

The patient with a duodenal ulcer will, during the period of his active symptoms, be awakened in the night by pain, depending on the quantity of food taken. If he has had a heavy meal he will awaken later than if the meal had been light. He is quickly relieved by bicarbonate of soda. The reverse is true of the gall-bladder patient. Such an individual will often state that if he eats late at night he can sleep the night through without disturbance. The reason is that the gall-bladder is generally most nearly full at the time the stomach is empty. When the gall-bladder is so distended, it gives rise to pain. Consequently, if a patient's stomach is full when he goes to bed and it takes six to seven hours to empty, the gall-bladder has no chance to become distended before the patient refills the stomach. Severe acute attacks of gall-bladder disease are most apt to come on at midnight and can generally be traced to a meal much of which was fried in fat. The very severe duodenal ulcer attack and sometimes the one with mild penetration come on during the day, one or two hours after a meal while the stomach is full.

There is generally no typical hunger pain with gall-bladder disease, a very important point in differential diagnosis. Although

there may be discomfort, distress or belching during the time of hunger—indicating that the hunger contractions are not unnoticed by the patient—actual pain is much more likely to result from gross motor disturbances at a time when digestion is at its height or when the stomach is full.

Gall-bladder pain radiates from the epigastrium to a corresponding point in the spine and spreads out from there to the entire back of the chest, and particularly to the right shoulder. When the pain of a severe gall-bladder attack does not radiate to the back of the chest, but is sharp and penetrating in character, it is associated with spasm of the diaphragm so that the patient chokes and feels he cannot breathe until relieved by morphin. His face becomes red with a cyanotic tinge, his eyes bulge and he is afraid to breathe. When we know such an attack has occurred diagnosis inclines toward gall-bladder disease.

At times, periodic severe attacks of pain in the right hypochondrium radiating to the right border and relieved only after the administration of morphin, fully simulating biliary colic, are present in the absence of biliary duct disease and are entirely due to chronic indurated or penetrating duodenal ulcer. In some of these patients each attack of pain is followed by mild icterus, which adds to the confusion of the clinical picture. These cases usually reach the operating table with a diagnosis of gall-stones and the surgeon finds an extensive duodenal or pyloric ulcer. The differential diagnosis is extremely difficult as even the objective examinations are not conclusive. The non-visualization of the gall-bladder with dye does not, of necessity, imply that the organ is diseased, because this may also occur when there is a duodenal ulcer. In some cases in our own series the preoperative diagnosis was gall-stones because the results of a thorough objective examination for gastric or duodenal ulcer were negative. At operation duodenal ulcer and not gall-bladder disease was found. These cases differ from actual severe biliary colic only in that most of the attacks occur during the day and are entirely independent of the time of eating. The particular reason a mistake is made in diagnosis is because the patient is entirely free of symptoms for weeks at a time.

Pyrosis, which is present during the florid stage of ulcer, is usually relieved by alkali. In gall-bladder affections it is present

most of the time, is not easily relieved, and is aggravated by fatty fried meals. As in functional hyperacidity, the patient takes larger and larger doses of alkali until he may become an alkali addict. The pyrosis in gall-bladder affection does not depend on the degree of hypersecretion. In fact, it has been demonstrated by Rehfuss and others that gastric secretions and acidity which are generally increased in duodenal ulcer may even show a diminution in the gall-bladder case. In gall-bladder disease, with gastric symptoms, it is hyperesthesia of the gastric mucosa that is responsible for pyrosis even with a low acidity. Whereas the inclination has been to regard gall-bladder disease as associated almost exclusively with subacidity, our own experience is that the greatest percentage has normal acidity. We have noticed hyperacidity in very few and actual anacidity in only one case.

The appetite of the ulcer patient is good. He is always willing to eat. The gall-bladder patient has a capricious appetite which, after protracted suffering, almost entirely disappears, probably due to the fact that the patient develops a subacid gastric catarrh, rarely a hyperacid gastric catarrh.

A history of reflex manifestations resulting from a disturbance in the vegetative system, particularly in the vagus, is more frequently encountered in gall-bladder affection than in peptic ulcer. These reflex phenomena are usually viscero-visceral disturbances.

The gall-bladder individual, in addition to his peptic ulcer symptoms, may at intervals, or persistently, suffer from vertigo. Von Bergmann explains this on the basis of the abdominal vagus carrying the impulses to the labyrinth. He speaks of gall-bladder vertigo analogous to Cushman's gastric vertigo.

In addition to peptic ulcer symptoms, the gall-bladder patient, particularly if obese, may have dysfunction of the islands of Langerhans, with mild glycosuria and even slight hyperglycemia.

Another symptom of great importance in some cases of chronic gall-bladder disease is the almost persistent pain in the right shoulder and right side of the chest, especially posteriorly, occasionally only in the right shoulder.

Objective Examination.—1. *Tenderness on deep pressure* is often elicited over the right hypochondrium. It is particularly marked when, in the process of palpation under the right costal border, the

patient is asked to take a deep breath. At the end of inspiration a sensation of pain is felt. This symptom may often best be brought out when the patient is sitting up or when lying on the left side, in which position the gall-bladder comes nearest the abdominal wall. Although the gall-bladder may not be directly palpable (unless considerably enlarged) it may be near enough to the palpating fingers to give rise to pain or palpation.

2. *Deep pressure pain*, if present over the right hypochondrium, is of diagnostic significance because in duodenal ulcer there is seldom tenderness on deep pressure, although there is usually marked tenderness on superficial pressure.

3. *Tenderness on percussion over the gall-bladder region* (Mendel's sign) is very rarely present in gall-bladder disease but is often positive in duodenal ulcer. Hence, it, too, serves as a diagnostic sign.

4. *Pressure over the right humero-clavicular joint* generally causes pain in this area when the gall-bladder is diseased. This is known as the Westphal sign. John Morley[15] attributes this symptom to the pressure exercised by a diseased gall-bladder on the serous surface of the diaphragm, causing radiation to the phrenic nerve. This would explain why a patient with gall-bladder disease, where there is irritation of the serous coat of the diaphragm, experiences pain in the shoulder on deep breathing, and it would also explain the spontaneous pain that is sometimes experienced in the right shoulder even when no pressure is exercised. Weiss and Davis[16] attribute these reflex pains to irritation in the segment of the cord situated higher than that which corresponds to the gall-bladder. In other words, it is a viscero-sensory reflex.

5. *Boas has described three sensitive pressure areas in gall-bladder disease*: (a) the seventh intercostal space; (b) a point to the right of the twelfth dorsal vertebra; and (c) over the right hypochondrium at a point intersecting a line running between the twelfth rib and the umbilicus. These signs are not as frequently positive in chronic as in acute and subacute gall-bladder affections. When positive in chronic cases, they are, of course, of great diagnostic value and hence should be looked for in every suspicious case.

6. *Enlargement of the gall-bladder*, if present, is a leading indication, but it is seldom encountered in chronic gall-bladder infections. The organ is contracted and not accessible to palpation in most cases

of chronic gall-bladder disease, particularly of a non-calculous type, or where there are only small calculi in the gall-bladder.

If the gall-bladder is enlarged and accessible to palpation, it is invariably diseased, because a normal gall-bladder is not palpable. One must be on his guard not to mistake an enlarged or ptosed right lobe of the liver for an enlarged gall-bladder. Careful palpation usually makes the differential diagnosis possible. The right lobe of the liver generally has a sharp edge and moves much more freely with inspiration than does the gall-bladder. At times the gall-bladder itself may be so markedly enlarged and bound down by adhesions that it simulates kidney or some other intra-abdominal tumor, such as cancer of the colon, retroperitoneal sarcoma or even hypernephroma. Cases are occasionally encountered where the size is so large that, although it is only chronically diseased, the gall-bladder reaches the pelvis, simulating ovarian growth. Such cases are extremely rare and occur chiefly in emaciated individuals or in individuals of congenital asthenic status.

7. *Enlargement of the right lobe of the liver* in connection with an indicative history is very important when one can exclude ptosis as a cause of the palpability of the liver. If it occurs in a woman with a pendulous abdomen or in an asthenic individual with ptosed organs, the entire liver border may be palpable and this fact is not indicative of gall-bladder disease. According to Graham[17] as well as Heyd, Killian and McNeal[18] the liver is co-affected in the majority of cases of extrabiliary duct affections, but this is still a moot question. Certainly, clinically, one may say definitely that in the vast majority of cases of uncomplicated chronic cholecystitis with or without stones liver affection is not the rule.

Enlargement of the liver or gall-bladder may be present in a number of intra-abdominal affections, particularly in duodenal ulcer during the florid stage. Therefore, such a finding must be weighed carefully.

8. *Cholesterol in the blood.*—The determination of this is very important, especially where there is evidence of cholesterol metabolism disturbance, such as obesity in a woman or feminine characteristics in a man. If these individuals have symptoms which are difficult to differentiate from peptic ulcer, the only positive guiding sign may be the increase of cholesterol in the blood. Individuals

who have considerable cholesteremia very often show xanthoma deposits on the upper and under eyelids. It must not be forgotten, however, that cholesterol increase may be present at times in conditions other than gall-bladder affections, especially in advanced arteriosclerosis.

9. *Urine Examination.*—Very often, if the urine of individuals with symptoms in the upper abdomen simulating those of peptic ulcer contains traces of sugar, the diagnosis is in favor of gall-stones and not of peptic ulcer, although one does encounter rare cases of ulcer of the lesser curvature which, because of dense adhesions to the pancreas, may so disturb the function of the islands of Langerhans as to give rise to mild glycosuria. We are inclined to agree with Seale Harris and Katsch that glycosuria and gall-bladder affections are not infrequently associated even to the extent that the glycosuria can be relieved, and true diabetes prevented, only if the gall-bladder is removed.

10. *Bilirubin and Icterus Index Findings.*—The blood for bilirubin and the determination of the icterus index are mentioned by some authors as important adjuvants in the diagnostic differentiation between peptic ulcer and gall-bladder disease, especially if an acute attack of pain in the upper abdomen gives rise to difficulty in judging as to whether it is due to peptic ulcer or cholelithiasis. In the latter, even in the absence of manifest icterus, the bilirubin—especially direct bilirubin—in the blood is increased. The icterus index is also moderately increased. In the acute case, these signs are not as reliable, for many cases have been reported where, during an acute attack in the upper abdomen when the pain was very severe, the increase in bilirubin of the blood proved to be present in association with peptic ulcer and absent in biliary colic. During the chronic state of gall-bladder disease, when the symptoms strongly simulate peptic ulcer, an increase of icterus index is a leading diagnostic sign.

11. *Non-surgical biliary drainage* advocated by Lyon[10-34] often furnishes very valuable diagnostic information. The bile is obtained in two receptacles under aseptic precautions. In choledochitis the first specimen is usually viscid, containing flaky mucus, pus-cells, epithelial cells and occasionally blood corpuscles. Bacteriologically, the culture may show different bacteria. In cholecystitis the first bile is normal but the second is viscid, flaky, turbid, and contains

stringy mucus, showing microscopically the products of inflamma-
tory changes. The cultures as a rule show pathogenic micro-organ-
isms. The color of the bile varies from deep golden-yellow to almost
a light mustard, turbid. Occasionally, it may be greenish, seldom
tarry. In the presence of gall-stones, there may be a gritty sediment
in the bile or it may be of a sand-like consistency. Microscopically,
evidence of crystals and bile pigments may be seen. Lyon observed
also, that acid is added to the bile. The bile may have a sparkling
character in case calcium and magnesium carbonate are present,
indicating the existence of stones in the biliary tract. Bockus found
that the cholesterol content of the gall-bladder bile is valuable com-
pared with that of liver bile, in determining whether or not the
gall-bladder empties itself. It serves as a fairly accurate gauge of
the bile-concentrating activity of the gall-bladder and of the presence
or absence of gall-bladder stasis.

The X-ray Examination.—The absolute value of the X-ray in
diagnosing gall-bladder disease has been firmly established by the
Graham method. It is unnecessary to elaborate on this method
here; it is universally utilized. It should be emphasized, however,
that the examination of the gall-bladder by the Graham method
should be preceded by the taking of films of the gall-bladder without
the dye (flat plate method).

The films should be taken in several positions, antero-posteriorly,
postero-anteriorly and, if the gall-bladder is situated very high, as in
the hypersthenic individual, so that it lies practically under the
lower border of the liver, in the erect position. Normally, the posi-
tion of the gall-bladder alters with the posture of the patient.

Recently, Cheray, Lomon and Albot[20] reported the results of
certain experimental and clinical work they had carried out regard-
ing a new position termed by them the left latero-anterior position.
When a patient lies on his back the gall-bladder moves up consider-
ably, is under the liver and remains on a line with the lower border
of the liver. It has exactly the same position encountered by the
surgeon at operation. When the patient is on the abdomen, the
gall-bladder is generally vertical. In the left latero-anterior position
the liver moves slightly to the left so that the space between the
kidney and the liver is almost vacant. The gall-bladder shadow
appears distinctly on the film and the gall-bladder is not covered by

the liver. Its density is more marked and one is sometimes enabled also to see the outline of the cystic duct. These French authors have recommended palpation in this position. We have routinely adopted this position in addition to the established positions. The method we employ is the following:[35]

The patient lies on the left side, the shoulders and hips in a straight line. He is then rotated to an angle of approximately 30°. Using the Bucky diaphragm and a cone, the average exposure is three seconds, five-inch spark gap, and twenty-five milliamperes, focused over the spine from the twelfth dorsal to the second or third lumbar region. The focus should be somewhat lower in thin individuals and a little higher in those who are stout, but one always focuses over the spine (Fig. 7).

Very often small calculi or even large cholesterol stones with a very thin capsule are better seen without the dye than with it. Furthermore, as pointed out by Snow,[21] hydrops of the gall-bladder often shows best without the dye. It is, in fact only diagnosticable if the gall-bladder is visualized on flat films. Kirklin[22] is of the opinion that the oral method is as good as the intravenous. He gives four grams of dye in the thirty cubic centimeters distilled water added to one glass of grape juice. It is taken immediately after an evening meal of the customary quantity, omitting fat. No food is permitted for sixteen hours after the taking of the dye. It is our practice almost invariably to administer the dye orally, giving two and five-tenths grams of the powder in orange juice at 8 P.M. or 9 P.M.; that is, two hours after the evening meal. It is important with some patients who become nauseous after the dye, to administer either some bicarbonate of soda in ice water, or have the patient lie on his right side for one-half to one hour after the dye is taken. No food is allowed until the patient comes for examination, not even tea in the morning. To prevent nausea, some use tincture opii, ten to twenty drops in water. One-one-hundred-and-twentieth grain of atropin by mouth one-half hour after the dye may also serve to prevent nausea in the very nervous individual. In the majority of cases, the patient overcomes the nausea spontaneously within a short time, although in a small percentage of cases the patient is so sensitive that he vomits the dye and thereby makes taking of the dye again necessary.

The preparation of the patient is very important. It is essential to clear the hepatic flexure of gas because when it contains a considerable quantity of gas this interferes with the filling of even a normal gall-bladder. Moreover, when a gall-bladder is thus filled, the outline is not distinct and other intestinal shadows or a fecal accumulation may simulate a filled gall-bladder. In such cases, reëxamination is essential.

To empty the bowel of its gas content, some recommend—in addition to a laxative the night before—an enema the morning of the examination. At one time we tried the administration of a tablespoonful of charcoal the night before the examination but without appreciable effect on the gas. In fact, it so often delays emptying of the colon that we have abandoned its use. If the patient is not very constipated, it is best to give him an enema the night before and another in the morning. A laxative often hastens the passage of the dye into the colon, delaying the reabsorption of the dye by the liver so that there may not be sufficient dye to enter the gall-bladder.

When we find on the film that the ascending colon is filled with dye, we do not regard this as an absolute indication of gall-bladder disease. We realize that the non-filling of the gall-bladder in such instances is probably not the fault of the gall-bladder mucosa or of the cystic duct, but is due to the fact that most of the dye is in the colon. It must be emphasized, however, that if repeated examinations show the dye in the colon with non-filling of the gall-bladder, the conclusion should be drawn that the dye could not enter the gall-bladder on account of cystic duct obstruction.

Blond,[23] who contends that the gall-bladder does not empty but that its contents are reabsorbed by the liver and that all the bile that reaches the intestines comes directly from the liver, utilizes the finding of dye in the hepatic flexure as a proof of his claim from both the physiologic and diagnostic standpoints. He says that normally if the cystic duct is open the gall-bladder takes up the bile. The substances that are not absorbed by the gall-bladder go back through the cystic vein into the hepatic vein and into the liver. If the cystic duct is obstructed or the gall-bladder mucosa thickened, the gall-bladder cannot take up the bile-containing dye. It passes, instead,

directly into the intestines and is seen in the hepatic flexure and ascending colon.

Whereas we agree that in some cases of cystic duct obstruction or disease of the gall-bladder mucosa, or both, the presence of a large amount of dye in the colon and none in the gall-bladder may be an indication of disease, the dye is nevertheless often found in the colon when the gall-bladder is not diseased.

We have stated elsewhere[24] that, based on the experimental work of others and our own clinical studies, we feel there is no doubt that the *greatest function of the gall-bladder is to empty part of its contents into the small intestines.* It is agreed by all physiologists that neither the lymphatic system in the gall-bladder proper nor its mucous membrane is of a character to indicate that the main function of the gall-bladder is resorption. Therefore, we feel justified in again calling attention to the important physiologic fact that the gall-bladder empties a good part of its contents through the cystic duct and sphincter of Oddi. It is quite likely that part of the contents emptied through the cystic duct are, as stated by Blond, taken up again by the liver through the cystic and hepatic veins, and it is easily understood that for body economy the liver takes up some of the substances contained in the bile. But this can only concern a small part of the bile that leaves the gall-bladder. The greatest part passes into the small intestines, some to aid in digestion, particularly of fat, and to stimulate pancreatic secretions, some to regurgitate into the stomach in order to lower and neutralize acidity, and some to pass into the colon.

Blond's assertion is that the folds of Heister prevent the gall-bladder's emptying itself into the cystic duct. In answer to the question as to how, then, is it possible for stones and sand to pass through the cystic duct into the intestine, Blond states that when the gall-bladder is in a pathologic state, the folds of Heister contract and do not hinder the outflow. This hardly seems tenable. Why one should attribute more importance to the valves of Heister as a control of the outflow of bile from the gall-bladder than to the sphincter of Oddi is very difficult to understand.

Regarding the diagnostic interpretation of dye in the hepatic flexure, without any dye in the gall-bladder, Blond rightfully states, "A normal gall-bladder shadow with a large depot in the hepatic

flexure indicates that the passageway in the papilla Vateri is normal, the hepatico choledicus is normal and the gall-bladder mucosa is normal. A faint gall-bladder shadow with a large depot indicates that the resorptive power of the gall-bladder mucosa is disturbed or that there is an increased resorption with a relative narrowing of the Heister valves or dilated hepatico choledicus. No gall-bladder shadow and a large depot means that the hepatic duct and the papilla Vateri are open and the gall-bladder is diseased."

No absolute conclusion can, however, in the absence of symptoms, be drawn from just one examination where a dye depot in the hepatic flexure is discovered with no dye in the gall-bladder. It should be the practice in these cases to reëxamine the patient eighteen or twenty hours after the administration of the dye. Often it will be found that by that time enough dye has been reabsorbed by the liver to fill the gall-bladder.

When judging the absence of the shadow of the gall-bladder, or its diminished density, one must observed whether or not the liver is filled with dye. If that is the case, it is necessary to wait another two or four hours before concluding that the non-filling of the gall-bladder is due to obstruction of the cystic duct or of the organ proper.

If the gall-bladder does not fill after all the foregoing precautions, one may conclude that either the cystic duct is obstructed or the mucous membrane of the gall-bladder fails to absorb the dye or that, as happens in rare instances, the large and small ducts of the liver are obstructed by thick bile that prevents the dye-containing bile from entering the gall-bladder.

In a very small percentage of cases the gall-bladder does not fill with dye despite the fact that the cystic duct is open and the mucous membrane intact. In these cases, generally some extrabiliary, intra-abdominal disease is present. One of the most common of such affections is pericholecystic adhesions either to the duodenum or to the hepatic flexure. Another condition is gastric or duodenal ulcer or a chronic appendicitis with dense adhesions in the ileocecal region. Recently, Bauer[25] reported cases of diabetes and thyrotoxicosis where the gall-bladder did not fill with dye. Crile, in an address before the New York Physicians Association, likewise stated that he had observed that in a certain percentage of cases of thyrotoxicosis peptic ulcer was also present. This should lead us in

those cases of thyrotoxicosis where the gall-bladder does not fill to suspect the coexistence of peptic ulcer. An explanation of why in thyrotoxicosis even a healthy gall-bladder may not fill is that the imbalance in the function of the vegetative nervous system that is present in thyrotoxicosis is responsible for existing abdominal symptoms. It is easily understood that in conjunction with this disturbance of functions of the digestive organs there can be sufficient disturbance in the biliary system as to interfere with the taking up of dye by the gall-bladder. Remarkably enough, Plumer (quoted by Kirklin[22]) has found that in a certain number of cases of myxedema the gall-bladder does not take up the dye.

In thyrotoxicosis and diabetes the non-filling of the gall-bladder with dye administered orally should be verified by dye given intravenously.

Other authors have reported cases where the gall-bladders of patients with mildly decompensated hearts with pain in the hepatic region failed to fill with dye. It is not possible to give a valid explanation of why the gall-bladder should not fill in these affections. It is likely that adhesions to the gall-bladder so disturb the function of its mucous membrane or the cystic duct that the gall-bladder can take up the bile normally coming from the liver but cannot accommodate itself to the foreign dye.

The failure of the gall-bladder to fill in some cases of peptic ulcer has been attributed to an excessive gastric acidity making the dye inert. This is not wholly satisfactory as an explanation because if it were true the dye ought to be made inert in the majority of cases, which is not so. It seems to us that in cases of positive peptic ulcer signs when the gall-bladder fails to fill, in order to exclude gallbladder disease the practice should be to introduce the dye through the duodenal tube, thus evading contact between the dye and acid secretions. The lack of filling of the gall-bladder in this small number of cases remains unexplained unless one is satisfied that in some cases of peptic ulcer there is a functional disturbance of the liver ducts with spasm of the sphincter of Lütkens. This may explain why some cases of peptic ulcer so strongly simulate gall-bladder disease clinically. Some authors assert that the non-filling of the gall-bladder in cases of peptic ulcer is an indication of some toxic liver damage, but this is problematic. It is also possible that the

individual afflicted with peptic ulcer is at the same time an outspoken vagotonic, with an associated imbalance in the function of the vegetative nerves of the biliary tract which interferes with the filling of the gall-bladder by the dye.

One can easily understand why in some cases of diabetes the gall-bladder may not fill. We are firmly convinced that in a fair percentage of cases of diabetes the gall-bladder is pathologic.

An explanation of non-filling of the gall-bladder in congestive heart failure is offered by Bauer to the effect that in connection with the general edema that is present, the gall-bladder mucosa is most likely edematous. We believe that an additional factor is probably the altered state of liver function, particularly of the liver ducts which meet with resistance in allowing the thick bile to pass. Hence the dye is not excreted into the gall-bladder. This explains why, in many of these cases, particularly mitral stenosis, bilirubin calculi and even mixed calculi may be encountered in the large duct and in the gall-bladder. In the presence of cardiac disease, it is best to accept the verdict of the oral administration of the dye rather than to substantiate it by the intravenous method. Further clinical studies should be the guide.

The non-visualization of the gall-bladder is, according to many authors, often encountered if the liver is diseased. The question as to whether or not the diseased parenchyma of the liver interferes with the passage of the dye through the ducts into the gall-bladder is a debated one. We are of the opinion that *the passage of the dye through the liver into the gall-bladder depends upon the integrity of the ducts and not on that of parenchyma proper.* If jaundice is due to disease of the hepatic cells but the ducts are free, the dye will pass and fill the gall-bladder. If the jaundice is due to disease of the biliary ducts the gall-bladder will not be visualized by the dye. Sodium phenoltetraiodophthalein (Iso-Iodekon, Mallinkrodt) is the dye advocated by Graham both to fill the gall-bladder and as a liver-function test.

If, in the absence of symptoms, the gall-bladder empties the dye after a Boyden meal, we have good reason to exclude gall-bladder disease. Occasionally, however, one meets a diagnostic disappointment. A dense shadow of the gall-bladder may be obtained with the dye, and yet operation will reveal a diseased gall-bladder. Therefore,

considerable importance attaches to the emptying and to the time of emptying of the gall-bladder. As a rule, a normal gall-bladder empties its contents one or two hours after a Boyden meal. If it remains entirely filled after the meal one may reasonably assume that its tone is disturbed. At times a gall-bladder that is considerably emptied after the Boyden meal may be refilled with dye twelve to twenty-four hours later. Occasionally the dye is retained in the liver, as evidenced by areas of dense shadows in parts of the liver and on this account the gall-bladder does not receive enough dye to cast a dense shadow. This condition must be carefully looked for before we attribute any diagnostic importance to the failure of the gall-bladder to be visualized by the dye, or to the fact that it is indistinct.

To facilitate the passage of the dye through the liver, it is advisable to give bile acids by mouth, best administered in the form of decholin (two tablets taken two hours after the dye and two more tablets the following morning). Some authors advocate the administration of one ampoule of decholin intravenously. The dye is given by mouth and an hour later the intravenous injection is given. This hastens the entrance of the dye into the gall-bladder so that it may be visualized in six to eight hours, when the shadow is dense.

In asthenic individuals, because of the atonic gall-bladder, an intramuscular injection of pituitrin the night before the dye is given is beneficial in emptying the gall-bladder so that it may take up the dye. This is based on the fact that in the atonic gall-bladder there is usually a stagnation of bile preventing its taking up the dye-containing bile. Pituitrin aids in emptying the gall-bladder and prepares it for taking up the dye. On this basis, pituitrin is also of therapeutic value in these atonic cases, as first pointed out by Kalk and Schoendube.[26]

Visualization of Calculi.—Very little need be said regarding the visualization of calculi. If these are definitely seen in a characteristic arrangement and outline, then the diagnosis is absolutely established. When the gall-bladder is not visualized by the dye and yet shadows are seen in the right hypochondrium, differentiation must be made between calculi and calcified glands or kidney stones, sometimes even between calculi and calcified costal cartilages, gas bubbles and fecal material in the hepatic flexure. Often small stones are

visualized in the form of mottling of the gall-bladder. Such mottling must be judged with care as gall-bladder mottling may be simulated by a part of the liver containing the dye or part of faecal-containing colon. Error is obviated if one notes the number of areas of mottling. If it is due to dye in the liver or fecal masses in the colon, more than one area is usually seen, whereas gall-bladder mottling is confined to a single, definite location.

Density.—If the density is not marked, this is not of necessity an indication of gall-bladder disease. The density depends upon how much dye enters the gall-bladder. The distribution of the density in the gall-bladder proper has been interpreted by some as indicating localized mucous membrane disease of the gall-bladder in the presence of an open cystic duct, but this should be judged with great caution from the diagnostic standpoint. It is important to remember that in the course of emptying of the gall-bladder, the density is more marked in the upper part than at the base, indicating that emptying does take place through the cystic duct. In our experience, as well as that of others, it has been found that often a very small gall-bladder may be an indication of marked contraction due to disease, or, what is more often the case, to partial filling of the gall-bladder, which indicates that part of the mucous membrane takes up the dye while the rest does not. Cases have been encountered where the organ is hour-glass in shape, the upper part of the hour-glass being much denser than the lower. This finding is an absolute indication of disease.

Irregularity of Outline of Border of Gall-bladder.—Irregularity of the outer border of the gall-bladder indicates pericholecystitis due, in the majority of cases, to gall-bladder disease. This is especially so if the gall-bladder is small and contracted.

Visualization of Deformed Gall-bladder.—Care must be exercised in the interpretation of a demonstrably deformed gall-bladder to decide whether the deformity is due to pressure from without, especially by large collections of gas in the colon, or to intrinsic disease of the gall-bladder. This is, as a rule, not difficult, because collections of gas pressing on the gall-bladder are usually detected by large dark areas within the hepatic flexure. The diagnosis of deformed gall-bladder is justifiable when a marked irregularity of the entire gall-bladder or localized deep contractions in the form of

an hour-glass are present without any surrounding areas of air bubbles (Figs. 8a and 8b, and Fig. 9). The visualization of adhesions of the gall-bladder to the adjacent viscera (especially to the stomach or duodenum) as a cause of symptoms simulating peptic ulcer is very often difficult. The reason for this is that after the stomach is filled with a meal the gall-bladder usually empties sufficiently as to make it impossible to detect adhesions between the pylorus or duodenum and the gall-bladder. That there are adhesions of the duodenum or pylorus to the gall-bladder may be deduced if the pylorus and duodenum are pulled upward or to the right, out of proportion to the rest of the stomach and to the status of the individual. If, in a person of normal status or one bordering on the asthenic habitus, the first portion of the duodenum and the pylorus are situated very high under the liver or to the extreme right of the median line, it is reasonable to assume that such adhesions exist. If the cap is serrated in its outer border or if its entire surface fills and is persistently irregular, one may deduce that there are adhesions between the cap and the gall-bladder.

Of great importance, also, is the appearance of the upper portion of the descending part of the duodenum. If this shows no corrugations and is considerably dilated, filling the lower part of the second portion in the form of a thin stream, one may also conclude with absolute certainty that the stagnation of barium in that portion is due to adhesions (Fig. 10). This conclusion is fortified if, fluoroscopically, regurgitation of contents from the second portion into the first portion is observed. This phenomenon, which we have often noted in adhesions, should not be confounded with retroperistalsis, seen in the second portion of the duodenum, and which is present normally in asthenic individuals with a high degree of ptosis and, in rare cases of spastic or organic stenosis between the second and third portions of the duodenum. Another sign of adhesions to the gall-bladder is when the descending portion of the duodenum is markedly curved or even V-shaped, with the apex extending to the right and the concavity inward.

The diagnosis of adhesions is still more justifiable if, under the fluoroscope, one finds that the mobility of the cap and the first portion of the duodenum is markedly restricted.

Indirect Roentgen Signs.—Very important information as to

Fig. 8a.

Deformed gall-bladder filled.

Fig. 8b.
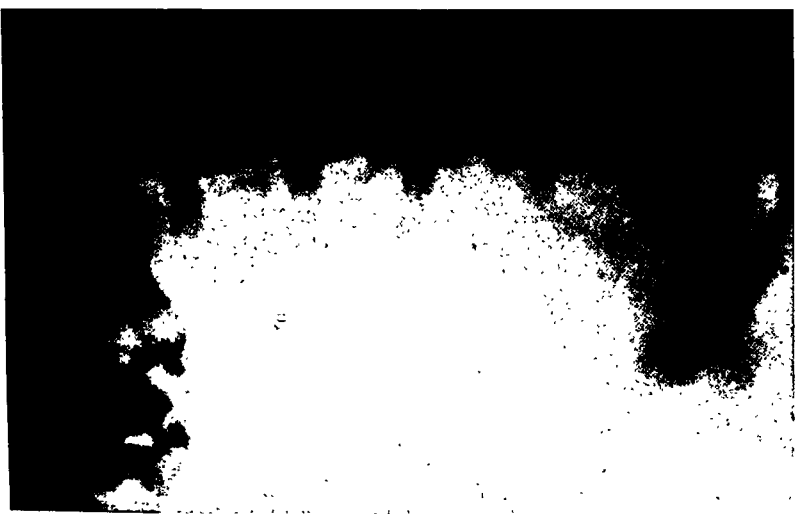
Deformed gall-bladder, same as Fig. 8a, emptied.

Fig. 9.

Fig. 10.

Hour-glass gall-bladder
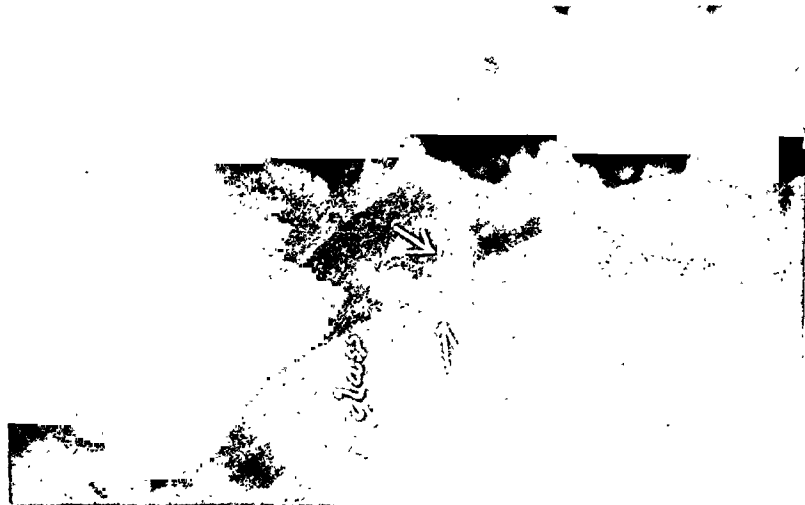
Distended upper part of second portion of duodenum due to adhesions.

whether the peptic ulcer symptoms are due to ulcer of the stomach or to gall-bladder disease is furnished by the so-called indirect X-ray signs. By indirect X-ray signs of gall-bladder disease, we understand such phenomena as are roentgenologically demonstrable in the stomach or duodenum and which are due to a diseased gall-bladder. These are by no means as valuable as the direct signs, but they must not be disregarded because they often give us a clue, not only to the fact that the gall-bladder is diseased but to an explanation of why symptoms of peptic ulcer exist.

The indirect X-ray signs are comparable to the subjective symptoms in contrast to the direct signs and objective symptoms. Subjective symptoms are transient, whereas objective symptoms persist. The X-ray phenomena of the stomach or duodenum which furnish indirect evidence of gall-bladder disease are likewise not persistent as a rule. They are usually present during the state of florid symptoms but during this time they are also very difficult to differentiate from peptic ulcer symptoms. This is especially true if the gall-bladder affection simulates ulcer high up on the lesser curvature with accompanying cardiospasm. If these symptoms exist, the cardio-spasm is so persistent as to mask all other signs and only an esophagoscopic examination and careful history-taking, together with the non-visualization of the dye by the intravenous dye method, will lead to a proper diagnosis. If the symptoms of gall-bladder disease simulate ulcer of the duodenum, the X-ray differential diagnosis is often made possible by repeated X-ray examinations of the duodenum.

Indirect Signs Pointing to Gall-bladder.—1. *Direct Deformity of the Duodenum Proper.*—This may consist of extreme spasm of the cap, giving it the characteristics of phthisis bulbi or it may resemble a clover-leaf or butterfly, or seem to be a pseudo-diverticulum on account of localized spasm. The most important point in the differential diagnosis is that no matter what its deformity, it is ultra-changeable, being present at one time and not at another. Even when persistent and due to spasm, it can be influenced by the administration of belladonna. In other words, it is a suggestive phenomena on the part of the duodenum.

2. *Spasm of the Pylorus.*—This, simulating pyloric ulcer with adhesions and a scar on the pylorus or a pivot-shaped pylorus, may be so persistent as to give rise to the alarming diagnosis of either

surgical ulcer or cancer of the pylorus. It is remarkable enough, that it is encountered in cases where the gall-bladder contains only one stone, but the gall-bladder symptoms are practically dormant and those of a gastric nature predominate.

3. *Spasm of the Sphincter Pylori.*—An extreme state of spasm of the sphincter pylori causing a marked dilatation of the entire pylorus simulating hypertrophy of the pylorus, a phenomenon often encountered in stenosing duodenal ulcer, is not infrequently present in gall-bladder disease (Fig. 11).

4. *Gastric Hyperperistalsis and Delay in Emptying of the Stomach.*—These indirect signs are less reliable than the foregoing and are much more transient. Delay in emptying of the stomach, if not explainable on the basis of stenosing pyloric or duodenal ulcer is in the greatest majority of cases present in gall-bladder disease with symptoms that are mostly gastric or duodenal.

IV. EPIGASTRIC HERNIA

A. V. Moschcowitz[27] was the first to draw attention to the frequency with which even a small epigastric hernia, detected only by most careful palpation, can give rise to symptoms simulating peptic ulcer. His assertions have proved correct in a great many cases. It cannot be emphasized too strongly, however, that at times these affections co-exist. Because of the frequency of this co-existence, it has occurred to us that there may be some relation between the occurrence of epigastric hernia and peptic ulcer. As pointed out by Moschcowitz, the symptoms of epigastric hernia are due to traction on the falsiform ligament of the liver which is subserous tissue. This may bring about a functional disturbance in gastric secretions and in gastric motility sufficient to cause symptoms simulating peptic ulcer. This is very important because if such irritation is permitted to continue it may eventually lead to actual peptic ulcer.

Epigastric hernia occurs much more often in men than in women. Diagnosis is established by carefully palpating—with one finger along the linea alba, beginning at the ensiform cartilage down to the umbilicus. If there is an epigastric hernia a small projection is detected slightly to the left of the median line. It is very tender to touch but, as a rule, does not give any impulse on coughing because it includes chiefly areolar tissue in the slit. The more marked her-

Fig. 11.
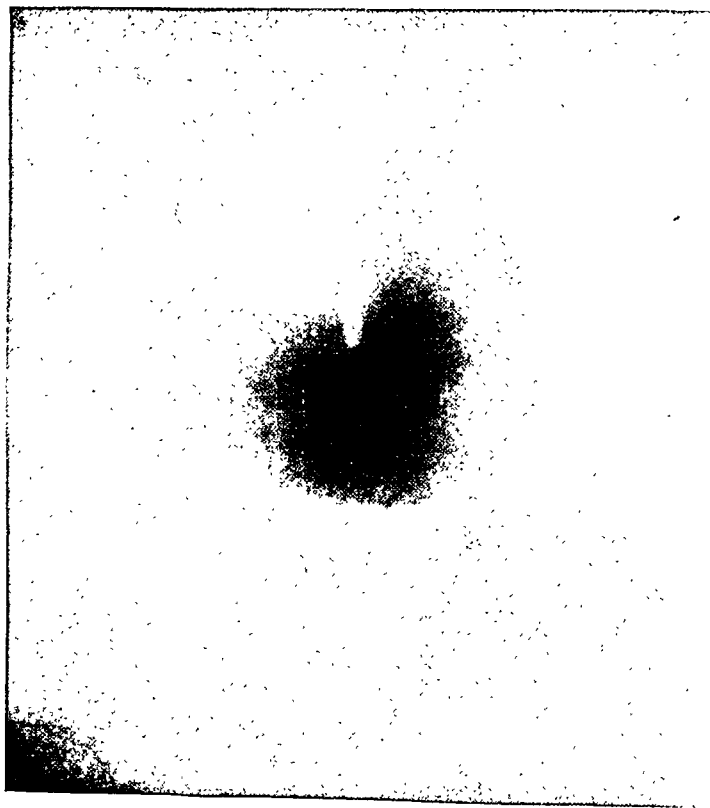
Pylorospasm simulating carcinoma.

nias, which give an impulse on coughing, may not give rise to as much pain and as many gastric symptoms as the smallest epigastric hernia. Such a small hernia should not be confounded, however, with the small fibrous nodules, neurofibromas or small lipomas which are generally much larger, multiple, and densely adherent to the skin. The foregoing palpatory finding, plus a careful X-ray examination of the stomach in order to exclude the presence of ulcer, justify a diagnosis of epigastric hernia.

V. COLICA MUCOSA

Colica mucosa is a condition characterized by periodic attacks of severe abdominal cramps relieved by evacuation of large casts of mucus. These are not mixed with stool and when examined microscopically are practically free from cells of an inflammatory nature except a few isolated eosinophiles. The condition is not inflammatory and should not be confounded with mucous colitis. The fact that the symptoms are periodic and that they are relieved by the discharge of mucous casts, the presence of eosinophiles in the mucous casts, and an occasional increase of eosinophiles in the blood during the stage of symptoms, led Strumpell to term this affection asthma of the colon. Nothragel, who first described it, considered it a purely secretory neurosis of the colon causing an increase in the mucus of the mucosa of the colon and the formation of mucous casts. This condition is often associated with disturbances of the vegetative nervous system and hence we have an explanation of why it gives rise to gastric symptoms closely simulating those of peptic ulcer.

The predominating gastric symptoms are usually those of gastric hypersecretion. There is a continuous regurgitation of sour fluid, the true complex of gastric succorrhea (Reichmann's disease). It is true that Reichmann's disease is, in the majority of cases, an expression of an existing duodenal ulcer, but it may also occur in the presence of colica mucosa, when it is most likely the result of duodenal irritation. The secretory symptoms are confined to the stomach whereas the sensory phenomena are chiefly confined to the lower abdomen. In most cases the pain is chiefly over the left side of the abdomen because the spasm predominates in the sigmoid colon, due in most cases to an extreme accumulation of gas in the splenic flexure but in some cases the pain arises from inherent spasm of the stomach

proper. The Roentgen examination of the stomach proper may be entirely negative or there may be evidence of duodenal irritation or where the splenic flexure is considerably filled with gas the so-called cascade stomach results. Whether the cascade stomach is entirely due to pressure or to associated spasm in regions of the stomach proper, or to both, cannot be stated definitely. It is our belief that where a cascade stomach exists it is an indication that there is both local and regional spasm. Local spasm causes an indentation on the greater curvature opposite the inciscura cardiaca with dilatation of the entire fornix. Regional spasm causes a narrowing of the pars media sometimes extending to the pylorus. The reason we believe that spasm of the stomach proper is a factor is because we often encounter cases with a great deal of gas in the splenic flexure or a large spleen or a large left kidney without an associated cascade stomach.

The differential diagnosis can be established only by a very careful X-ray examination of the stomach to exclude peptic ulcer. In the majority of cases the stomach will show persistent spasm of the entire sigmoid and often an associated spasm of the caecum and ascending colon. In the majority of cases, however, the caecum is dilated. Some authors have described the frequent association of a cascade stomach with this affection. It occurs most often in asthenic individuals. Very often careful palpation in thin individuals reveals a cordlike descending colon.

VI. CALCIFIED MESENTERIC GLANDS

A condition that occasionally gives rise to peptic ulcer symptoms is the presence of mesenteric tuberculous glands usually situated high in the upper part of the abdomen. In English medical literature the importance of the fact that such enlarged tuberculous glands in adults gives rise to peptic ulcer has long been emphasized. Recently, in this country, Auchincloss[28] called attention to their presence as being of surgical importance, and also to the fact that they give rise to peptic ulcer symptoms as well as to other intra-abdominal symptoms. The diagnosis is best established by the taking of films of the abdomen before the contrast meal is given and carefully noting whether or not such calcified glands are present in the abdomen and, if they are, their location.

VII. BOTHRIOCEPHALIS LATUS

A peculiar and unexplained condition occasionally simulating peptic ulcer is the presence of a tapeworm. We have encountered several cases of this nature where the symptoms were entirely those of peptic ulcer. Only after the patient himself had noticed segments of the tapeworm was our attention directed to the possibility that the cause of the symptoms was not peptic ulcer. In two of the patients whom we have followed for several years, the successful removal of the tapeworm brought about the complete disappearance of the peptic ulcer symptoms. We mention this affection here because it is a disease seldom thought of in this country and yet its possibility should not be overlooked.

VIII. ANGINA PECTORIS

Peptic ulcer situated high on the lesser curvature accompanied by marked cardiospasm may give rise to symptoms closely simulating angina pectoris. This may be so much the case that differential diagnosis is impossible. There may be neither positive evidence of peptic ulcer nor of coronary disease or disease of the aorta. Cases have been reported in the literature, and we have also encountered some, where a long history pointed to angina pectoris, yet, during the course of treatment for this disease, the actual diagnosis was suddenly disclosed by a gastric hemorrhage. At times an ulcer of the pars media, pylorus or duodenum may give rise to symptoms of angina pectoris.

IX. TABES DORSALIS

A disease from which peptic ulcer must be differentiated is gastric crisis in the course of tabes dorsalis. This is, of course, not difficult if the crisis occurs in a typical manner; namely, periodic severe attacks of cramps in the upper abdomen with persistent vomiting of gastric secretions, total loss of appetite, and rapidly progressing emaciation. It is much more difficult to differentiate the conditions where the gastric crisis symptoms are less severe and have the characteristics of peptic ulcer. In addition to the hunger pain, gastric hemorrhage may occur in the course of the crisis without the presence of peptic ulcer. If the routine examination does not neglect inspection of the pupils and the knee reflexes as well as the

Wassermann reaction of the blood and a spinal fluid test, a mistake in diagnosis is hardly possible.

There are cases, however, of gastric crisis in which the gastric symptoms predominate and the ulcer phenomena are either so vague or absent that unless a most thorough examination of all the nervous phenomena is made the diagnosis is very often missed. This is especially so if the luetic lesion is still limited to a localized area in the dorsal region of the cord where the lumbar and cervical regions of the cord are practically free so that the knee and pupillary reflexes are still normal. In these cases, a careful examination for areas of anesthesia in the region of the nipples will reveal the presence of concealed tabes dorsalis as the cause of the gastric symptoms. An important guide to diagnosis is the presence of sub- or anacidity or even achylia gastrica. Whenever one encounters persistent gastric symptoms out of proportion to the physical findings with sub- or anacidity or achylia gastrica present—even in the absence of a positive Wassermann blood reaction and spinal fluid—one is justified in treating the case on the basis of lues. It has been conclusively shown by Brugsch and Schneider[20] that the tabetic spinal symptoms may be long preceded by gastric symptoms with sub- or anacidity and these authors emphasize the need of instituting treatment at this time in order to prevent the more serious spinal symptoms.

A luetic individual even with early signs of tabes may, of course, also have a peptic ulcer which need not be on a luetic basis. It seems to us that pure luetic ulcers, although occasionally encountered, are extremely rare. This is mentioned because if a tabetic individual happens to have a peptic ulcer not due to lues and the lues is practically in a dormant state, the ulcer will not only fail to benefit by anti-luetic treatment but the symptoms may be aggravated. We encountered one case of tabes dorsalis with gastric symptoms who. had repeated gastric hemorrhages but because of the tabes dorsalis his gastric symptoms were treated on a luetic basis. As he did not improve he eventually had to be operated upon, at which time a large ulcer was found and resected with the patient making a complete recovery not only from the operation but from his gastric symptoms.

Is there any roentgenologic evidence which can differentiate as to whether gastric symptoms are of tabetic origin or due to ulcer?

The X-ray may be characterized by marked hyperperistalsis with localized persistent indentations along the greater curvature as first pointed out by Groedel.[30] Some authors state that gastric symptoms due to crisis are characterized by extreme spasm of almost the entire stomach, being so marked as to simulate linitis plastica or scirrhus carcinoma of the stomach. In other cases where there is actual deformity of the stomach due either to the scars caused by lues or to gumma or to ulceration, differentiation is much more difficult. If due to gumma, the X-ray evidence may simulate carcinoma of the stomach and only a positive Wassermann reaction and the success of the anti-luetic treatment can clear the diagnosis. If due to excessive connective tissue formation with large scars, marked deformity of the organ is present and, according to Lewald[31] the so-called dumb-bell stomach results. There are, however, cases where the connective tissue may be confined to other parts of the stomach, causing the most varied deformities. The feature that should awaken suspicion of a luetic origin of the gastric symptoms is the fact that the irregular areas are not localized as in ulcer or cancer, but are scattered throughout the stomach. Finally, where there is ulceration without scarring and deformity the roentgenologic evidence may be exactly like that of ulcer of non-luetic origin. When one encounters roentgenologic evidence of extreme atony of the stomach in addition to the presence of an ulcer niche and marked delay in emptying of the stomach not the result of pyloric stenosis but due to associated atony, suspicion should be awakened that the ulcer is on a luetic basis. We do not base this statement on an extensive experience, but two cases of this nature have impressed us with the importance of this phenomenon.

Additional aid in establishing the diagnosis is furnished if the thoracic aorta is dilated, particularly the ascending portion and arch, and shows the characteristics of or a suspicion of luetic aortitis. There is no doubt whatsoever that when tabes dorsalis gives rise to gastric symptoms luetic aortitis is nearly always present, although not of necessity giving rise to clinical symptoms.

X.   DUODENAL IRRITATION

Sometimes a great deal of difficulty is encountered in the differential diagnosis between duodenal ulcer and duodenal irritation, espe-

cially if, in addition to the subjective symptoms, roentgenologic evidence speaks for some disturbance in the duodenum. It is well known that frequently the first portion of the duodenum or the cap is accused of having an ulcer with only the slightest roentgenologic evidence to support the accusation. It is therefore no wonder that Cole, Ackerlund, Hurst, and others insist that the X-ray diagnosis of duodenal ulcer be made only if deformity pointing to the seat of the ulcer is present. However, one actually does encounter cases with symptoms strongly simulating duodenal ulcer with such vague and transient duodenal X-ray signs that it is very difficult to state with certainty whether or not an ulcer is present. We are in accord with Barclay[32] who speaks, in these cases, of duodenal irritation. Kirklin[33] speaks of it as duodenitis. It is important to remember that the symptoms are not due to ulcer and that these patients should not be subjected to surgical treatment. The leading X-ray signs of duodenal irritation in the absence of ulcer are that the cap either fails to fill, or, should it fill, does so very transiently and empties very rapidly; or, the barium may be scattered, not filling the duodenum completely. Even when the patient is watched fluoroscopically and the barium contents are pressed into the duodenum by the palpating hand one sees the duodenum empty itself almost at once. At no time is any actual deformity present and certainly there is no niche. The reason a hasty observation may mistake the condition for ulcer is because a fleck may be persistently present in the duodenum and sometimes an indentation due to spasm of the greater curvature may be seen. In some cases roentgenologic diagnosis is rendered especially difficult because this fleck persists after the stomach is empty, four or five hours after the meal, and because the pyloric canal may be eccentrically located. In such cases only repeated examinations and particularly the examination of the patient after the subsidence of his symptoms will lead to a proper diagnosis.

SUMMARY

Based on clinical experience, we have tried to analyze with as much exactness as possible those conditions which closely simulate peptic ulcer and on account of which treatment may be wrongly directed to peptic ulcer. The recognition of these diseases and the removal of their causes often eliminate the symptoms simulating

peptic ulcer and serve to prevent the formation of an ulcer. In those diseases, such as chronic appendicitis or gall-bladder affections, simulating peptic ulcer where surgical intervention alone can relieve the symptoms, it must be remembered that it may be necessary for some time after the appendectomy or other surgical procedure to carry out medical treatment directed toward the gastric symptoms. Where this is not done and the gastric symptoms persist, opportunity is furnished for critics to state that the organ removed was not the actual cause of the symptoms. If the diseases outlined are borne in mind and all diagnostic methods at our disposal are employed, a proper diagnosis will be arrived at in a majority of cases.

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SUBACUTE RECURRENT DUODENITIS: CLINICAL AND ROENTGENOLOGICAL CONSIDERATION

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THE subject of duodenitis as a distinct disease entity has received meager recognition among the gastro-enterologists and especially so among the general practitioners. In reviewing the literature of the past decade, one can find only occasional reference made to this condition, and this only in a more or less casual manner. Insufficient emphasis is placed upon its frequency, importance of diagnosis and prophylactic treatment, bearing in mind that the actual pathology that this condition presents is little short of a pre-ulcer stage, if not in the majority of cases culminating in an ulcerous condition, presenting the well-known duodenal ulcer syndrome. While it is a known fact that a peptic ulcer of the stomach or the duodenum is generally associated with a certain degree of inflammatory reaction of the surrounding mucosa, so is it as equally conceivable that a generalized inflammatory state of the duodenal mucosa will, in many cases, predispose that part of the intestine to ulceration.

Before discussing duodenitis from the clinical and roentgenologic standpoint, it would not be amiss to elucidate upon the term "duodenitis," and draw a distinct line of demarcation from the description of this condition as given in the text-books. In fact, from a careful study of the history, X-ray and other findings, one is tempted to designate a name for this condition which would be more descriptive of its actual pathology and clinical course. It would seem that a term "subacute recurrent duodenitis," such as I have coined for this paper, is more appropriate than the vague term, duodenitis, used by various authors to describe a disease entity, which may or may not conform with the description of the cases given in this communication.

The chronicity of the average case seen, the intervals of complete freedom from pain and its recurrent nature, characterize the condi-

tion. The pain, which may be very severe, very frequently simulates ulcer pain, appearing with regularity and showing definite food and soda amelioration. Roentgenologically, however, no definite evidence of duodenal ulcer can be found, but certain signs are discernable, which we must recognize as deviations from the normal, and indicative of pathology in the duodenum. The stomach frequently shares the irritability of the duodenum and sometimes shows very definite pathology. This is clearly demonstrated in Case 3 of the present series. Irritability of the duodenal bulb is a constant and marked feature; the latter is unable to hold the barium, resulting in rapid emptying. This phenomenon accounts for the difficulty which one encounters in attempting to fill the bulb. The bulb is usually, but not constantly, deformed, diminished in size, and its margins tend to be hazy and indistinct. At times the bulb' has a mottled appearance, with spastic deformities, giving its margins a serrated form. These deformities are not constant in the same case, the cap changing its appearance from time to time, seldom assuming normal outlines. The descending portion of the duodenum shows evidence of either a loss of normal rugal markings, appearing dilated, or one may observe marked spasticity with apparent narrowing of its lumen and evidence of peri-duodenal adhesions. This entire portion of small intestine frequently shows an uneven distribution of barium due to spastic phenomena. Case 9. illustrates this involvement of the first and second portions of the duodenum, showing evidence of peri-duodenal adhesions and a large diverticulum in the second portion.

There was nothing noteworthy in the gastric chemistry of those cases; the acid values may be within normal limits or show an increase. Blood was found in three instances, in one case macroscopic blood was found in the gastric contents on several aspirations.

In order to more closely familiarize one with the symptomatology of duodenitis and sufficiently evaluate its frequency, it would not seem amiss to briefly cite some case histories. The latter is of paramount importance in corroborating roentgenologic findings.

CASE 1.—E. S., female, aged twenty-six, referred by Dr. M.O. Her chief complaint is pain in the epigastrium and right hypochondrium radiating to the intrascapular region, apparently having no distinct relation to meals, but at times is relieved by food. She also experiences a dull, dragging pain in the

FIG. 1.—(Case I, page 247.)   FIG. 2.—(Case II, page 247.)
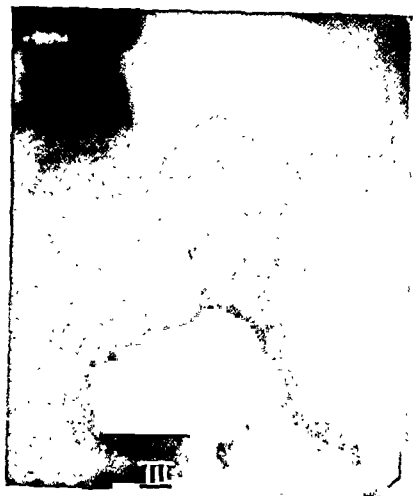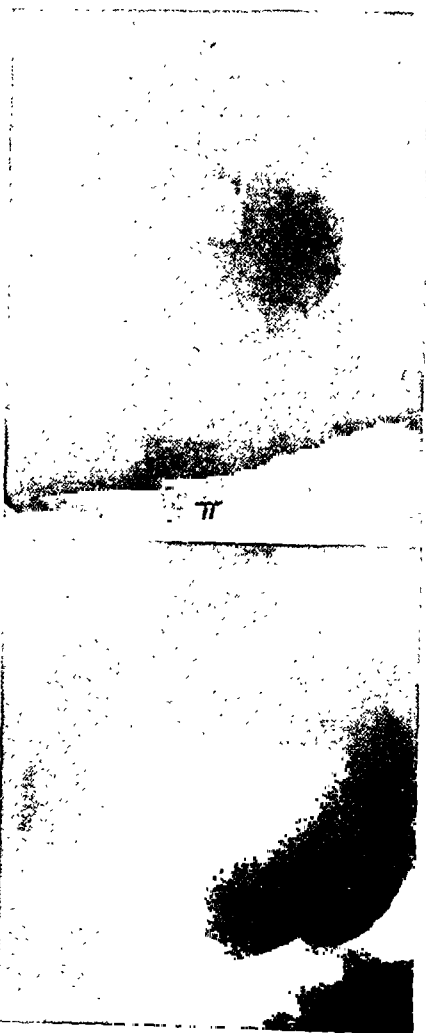
FIG. 3.—(Case III, page 248.)   FIG. 4.—(Case IV, page 248.)

For interpretations of the skiagraphs, see descriptions in text.

right iliac fossa. Two days ago she was awakened at 2 A.M. with the above-described, severe pain, which lasted about an hour, being relieved by a hot-water bag. Past history is negative except for a tonsillectomy five years ago. Present complaint dates back to seven months ago. During this period she had complete freedom from pain, lasting almost three months, with recurrence of symptoms which are much more severe. Physical examination reveals a rather self-conscious, neurotic type of patient. Heart and lungs are negative. Abdominal examination elicits some tenderness over McBurney's point and in the right hypochondrium. Gastric analysis reveals acid figures within normal limits. No blood in the stool. Roentgenologic examination (Fig. 1) reveals a gastric hypermotility with marked hypermotility of the duodenum. The duodenal cap appears spastic and irritable, showing inconstant deformity with marked tenderness on palpation. In view of the findings, a diagnosis of duodenitis was made. The patient responded almost immediately to a modified ulcer diet and alkalis.

CASE 2.—S. H., male, aged twenty-three, referred by Dr. S.C.R. His chief complaint is pressure in the epigastrium with sensation of fulness after meals, and feeling as if food would lodge in the epigastrium. He experiences frequent attacks of nausea, dizziness and belching, these symptoms coming on one to two hours after meals, and associated with an apparent inability to take full inspirations. Present complaint dates back to five months ago; at that time similar symptoms lasted several weeks. They disappeared completely to return a week ago, following a heavy meal. He admits being a hardy eater. The past history, with the exception of a fractured skull twelve years ago, and a herniotomy a year ago, is irrelevant. Physical examination reveals a highly neurotic, sthenic type of patient. Chest is negative. Abdominal palpation reveals some tenderness in the right hypochondrium, otherwise negative. Gastric analysis shows normal acid values; a good deal of mucus is present. X-ray examination reveals (Fig. 2) a gastric hypermotility, an indistinctness and haziness of the distal third of the pars pylorica, at both curvatures, and many small spastic incisuras, especially marked along the greater curvature, giving the outlines a serrated effect. The duodenal bulb is small and spastic, fills with difficulty and displays marked irritability, manifesting itself in rapid emptying. The entire bulb displays a certain degree of haziness. A diagnosis of prepyloric gastritis and duodenitis was made. The patient showing marked improvement on the proper diet and medication. This case is illustrative of the fact that the gastric mucosa, especially the pyloric portion, in some cases participates in the pathology existing in the duodenum.

CASE 3.—H. W., male, aged thirty-eight, was first seen in May, 1927. His chief complaint at the time was epigastric pain and distress about one to two hours after meals, associated with nausea and occasional vomiting. The pain is relieved by food and somewhat by alkalis. The above complaint dates back to a year ago, the pain then being of brief duration, and not quite as severe. The physical examination is essentially negative, except for marked tenderness in the epigastric region, the patient displaying evidence of being high-strung with neurotic tendency. Examination of the gastric contents revealed high acid values and absence of blood. Roentgenologic examination at that time revealed a stomach which was markedly hypertonic, displaying hyperperistalsis and hypermotility. The duodenal bulb was extremely spastic, showing marked irri-

tability, yet not persistently defective. Sufficient evidence for a positive diagnosis of ulcer was lacking. In view of the symptoms, the patient was placed on a bland diet, alkalis and antispasmodics, with complete relief of symptoms for almost two years. In April, 1929, he was seen again, the symptoms having recurred. The pain this time is not as severe, but nausea and vomiting one to three hours after meals are quite marked. Gastric contents show a total acidity of 48 degrees and 32 degrees of free hydrochloric acid; an appreciable amount of macroscopic blood and mucus were present on aspiration. X-ray examination at this time (Fig. 3) reveals marked hyperactivity of stomach and duodenum. The lesser curvature displays spastic irregularities and evidence of a hypertrophic gastritis. The duodenal bulb is extremely spastic, of hazy outline, showing rapid emptying and inability to hold the barium. A diagnosis of subacute gastro-duodenitis was made, and the patient again placed on a suitable diet, medication and gastric lavages, with complete disappearance of symptoms to date.

CASE 4.—C. C., male, aged sixty-five. Was first seen September, 1929, complaining of pain in the epigastrium, radiating to the left lower chest, appearing one to two hours after meals, especially after eating solid foods. The pain at times wakes him from sleep, and is relieved by the ingestion of soda. Associated symptoms are abdominal bloating and vomiting two to three times weekly. This he usually had to induce, in order to relieve nausea and epigastric distress. Past history: had similar symptoms five years ago, with hematemesis on one occasion, condition at the time lasting several weeks. He felt well until a year ago, when, he believes following a dietary indiscretion, the symptoms recurred, and have been intermittently very severe. He claims to be a heavy eater. Physical examination reveals a senile, well-preserved individual. Chest is negative. No masses felt in the abdomen or tenderness elicited. Gastric analysis reveals absence of free hydrochloric acid, and presence of fresh blood, probably due to trauma. X-ray examination (Fig. 4) reveals an irritable and spastic duodenal bulb, showing marginal haziness and serration, so typical of duodenitis, without definite roentgenological signs of ulcer. Dietary control, plus alkalis, antispasmodics and sedatives influenced this case favorably, though not completely. Slight dietary indiscretions were sufficient to provoke symptoms.

CASE 5.—J. S., male, aged thirty-two. His chief complaint is pain in the epigastrium two to three hours after meals, relieved by food and soda. Associated with the above are belching and sensation of pressure in the epigastrium after meals. The above symptoms made their appearance two and one-half years ago, during which time he had several periods of intermission, of longer or shorter duration, with complete freedom from pain. At present the pain is more severe and frequent, his appetite rather poor, although, before the present illness, he had been wont to partake of heavy meals. Past history is irrelevant. Physical examination reveals nothing of importance. Gastric analysis shows high acid values—total acidity 88 degrees, free HCl 52 degrees, no blood found. X-ray examination (Fig. 5) reveals a gastric and duodenal hypermotility; the first and second portions of the duodenum are somewhat dilated. The duodenal bulb presents evidence of irritability and transient spastic phenomena. In view of the history, symptomatology and roentgenologic findings, the latter showing

Fig. 5.—(Case V, page 248.)

Fig. 6.—(Case VI, page 249.)
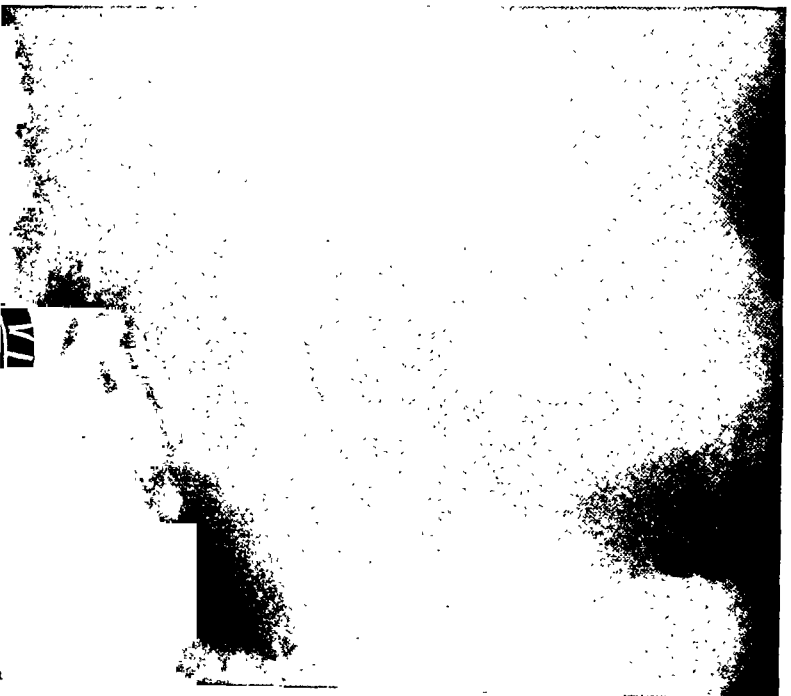
For the interpretations of the skiagraphs, see descriptions in text.
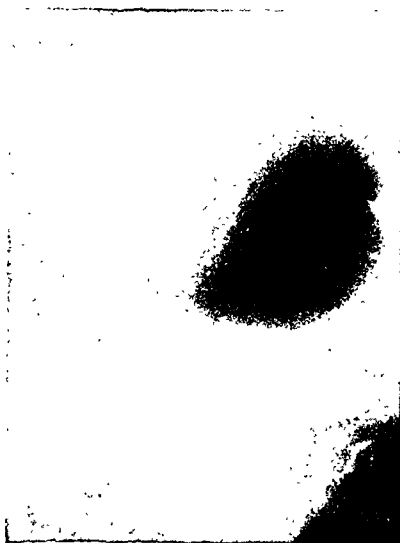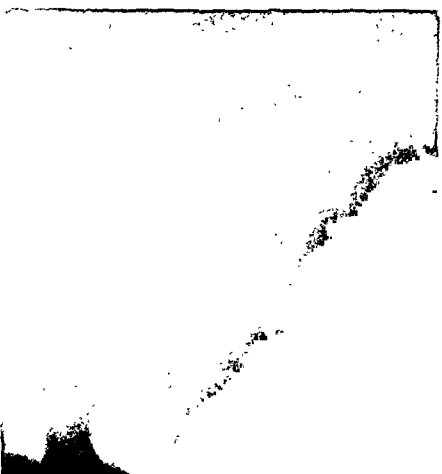
For the interpretations of the skiagraphs, see descriptions in text.

no evidence of ulcer, a diagnosis of duodenitis was made. Patient responded very favorably to treatment.

CASE 6.—A. W., male, aged thirty-eight. His chief complaint is pain in the epigastrium, boring in nature, appearing one to three hours after meals, relieved by alkalis and food. The pain is quite severe when hungry. Belches excessively, especially after meals. He is a heavy eater and uses tobacco to excess. Duration of present symptoms is two months. He had similar pains one and one-half years ago, but not as severe. Past history is essentially negative. Physical examination reveals nothing of importance. Gastric analysis shows normal acid figures, no blood found. X-ray examination (Fig. 6) shows duodenal irritability. The duodenal cap displays haziness and spasticity along the superior and lesser curvature margins, with rapid emptying. A diagnosis of duodenitis was made, with good therapeutic results.

CASE 7.—A. F., male, aged forty-seven. His chief complaint is pain in the right and left hypochondrium, appearing three to four hours after meals, and associated with abdominal bloating, belching and pyrosis. Past history is essentially negative. Present illness dates back to eighteen years ago. During this period he had free intervals lasting as long as two years. The present recurrence is of four months' duration, and appears to be of greater intensity. Physical examination reveals some tenderness in the epigastrium and over the pyloric region. Patient is highly neurotic and introspective. Gastric analysis shows normal acid values, large amount of mucus and absence of occult blood. Stool is negative for blood. Roentgenologic examination (Fig. 7) reveals no evidence of gastric pathology. The duodenal bulb appears spastic, very irritable, hazy in appearance, and shows deformed outlines apparently due to peri-duodenal adhesions. In view of the findings a diagnosis of duodenitis with probable peri-duodenal adhesions was made. The patient, however, did not seem to improve on the usual duodenitis régime. This may be attributed to the fact that the pathologic process has progressed to the stage where the entire duodenal wall is involved, with peri-duodenal pathology.

CASE 8.—H. L., male, aged forty, referred by Dr. S.J.M., his chief complaint being a cramp-like pain in the para-umbilical region, which does not radiate, coming on usually before meals, relieved by food. He also experiences epigastric fulness and discomfort after meals. The past history is essentially negative. Present complaint dates back to three weeks ago, during which time he lost seven pounds as a result of dieting. Physical examination and gastric analysis show nothing of importance. Roentgenologically (Fig. 8) the stomach appears normal. The duodenal bulb is small in outline, appears hazy, and displays irritability and repeated spastic phenomena. A diagnosis of duodenitis was made, the patient responding well to treatment.

CASE 9.—F. R., female, aged twenty-one. Her chief complaint is pain in the epigastrium, appearing about one hour after meals, relieved by food and alkalis. Belches and regurgitates food frequently. Suffers from anorexia and severe nausea, especially mornings, and is markedly constipated. Lost six pounds in the past few months. Past history is essentially negative. Present complaint dates back to a year ago; at the time similar symptoms made their appearance, lasting about three months, and disappeared completely, to recur five weeks

ago. Physical examination reveals an asthenic type of patient; some tenderness is elicited in the epigastrium and right iliac fossa, otherwise negative. X-ray examination reveals a marked gastric hypermotility and hyperperistalsis. The duodenal bulb appears dilated, is irregular in outline, which is not constant, and displays irritability. The second portion of the duodenum shows the presence of a diverticulum (Fig. 9), about the size of a walnut, with a six-hour barium retention. The third portion of the duodenum is dilated and displays evidence of peri-duodenal adhesions. The patient's symptoms were controlled promptly on a bland diet and proper medication.

This case is of interest from the standpoint of the definite pathology it presents throughout the entire duodenum. The diverticulum and the peri-duodenal adhesions may well be considered as the sequelae of the duodenitis.

CASE 10.—I. F., male, aged thirty-one, referred by Dr. Wm. G. His chief complaint is pain in the epigastrium radiating to the right hypochondrium, appearing when he is hungry, or about two hours after meals. Food gives him considerable relief. Associated symptoms are epigastric bloating, belching and occasional pyrosis. He had similar symptoms two years ago, lasting several months, with complete remission, and a second recurrence about a year ago lasting several weeks. The past history is irrelevant except for an orchitis sixteen years ago. He is accustomed to partaking of large meals and highly seasoned foods. Physical examination is essentially negative. X-ray examination (Fig. 10) reveals a gastric hypermotility and irritability of the duodenal bulb, the latter having a skeleton-like appearance, alternating with complete filling from time to time. No evidence of ulcer could be found. A diagnosis of duodenitis was made, the patient responding favorably to the usual treatment.

Discussion.—What criteria are we to be guided by in diagnosing a case of duodenitis? That this entity exists is a well-established fact. Judd, in 1921, described a condition manifesting peptic ulcer symptoms, the mucous membrane of the duodenum, when the bowel was opened, showing localized or diffuse inflammatory areas, the mucosa bleeding easily on manipulation. Eastmond, in a very comprehensive communication on roentgen manifestations of gastro-intestinal infection, describes the roentgenologic signs of duodenitis, and stresses the importance of recognizing them as being produced by pathology within the duodenum. Very frequently, indeed, such cases are overlooked, the symptoms, in view of the fact that definite evidence of ulcer is lacking, are attributed to a functional, reflex or secretory disorder of the gastro-intestinal tract, and the failure of properly evaluating minute radiographic deviations from the normal, and correlating such findings with a proper history, merely aids to the inability of establishing a proper diagnosis and subsequent therapeutic management.

Kirklin recently reported a series of forty-five cases of duodenitis, pointing out the fact that clinically these cases did not present salient features of distinction from duodenal ulcer cases. Symptomatically, I am inclined to divide cases of duodenitis into two groups: (1) those presenting the typical duodenal ulcer syndrome; and (2) cases of shorter duration with a less defined symptomatology. The latter group cases usually complaining of vague, upper abdominal discomfort after meals, abdominal bloating, belching, nausea, vomiting and dizziness. An interesting symptom in some cases is their inability to fully complete the act of inspiration. This is probably a neurotic manifestation, which is rather pronounced in a good many of these patients. An important point worth mentioning here is the fact that many of these cases are usually heavy eaters. Judging from the above data, a diagnosis of subacute recurrent duodenitis should be based upon the following considerations: (1) history conforming with one of the two symptom groups above described; (2) roentgenographic signs characteristic of duodenitis, and lacking evidence pointing towards existence of duodenal ulcer; (3) the ruling out of extra-duodenal or gastric factors which may be responsible for reflex phenomena within the duodenum, such as disease of the gall-bladder, appendix or colon. One must 'stress the importance that only by correlating the above findings, can we arrive at a positive diagnosis in, perhaps, the majority of these cases.

Etiology.—As to the etiology of subacute recurrent duodenitis, nothing definite can be stated; it is highly probable that the factors operative in the production of peptic ulcer may also be responsible for this condition. Nickel, in a recent communication, claims to have consistently isolated from various foci of infection, and from the surgically removed tissues, from cases of duodenitis and peptic ulcers, a streptococcus like the one isolated and described by Rosenow. These organisms have been shown to produce ectotoxins and endotoxins which specifically affect the gastric and duodenal mucosa. Dietary indiscretions and excessive smoking seem to play important rôles as causative factors. These superimpose injury upon a pre-existing infected mucosa.

Treatment.—In view of the nature of the existing pathology, it is quite apparent that the treatment of duodenitis is entirely medical, the majority of patients responding promptly to a bland, smooth

diet. Frequent feeding of small quantities of food is indicated in patients displaying more acute symptoms. Alkalis, anti-spasmodics and sedatives should be resorted to when necessary. In refractory cases, trans-duodenal lavages, with warm saline or silver solutions, three to four times weekly, in addition to the above measures, have proven of value. Eradication of suspicious foci of infection and restriction to tobacco is imperative. These patients must be under rigid medical supervision for a period of at least one year.

Summary.—Duodenitis as a distinct and frequent disease entity is herein described, and its more frequent recognition among the gastro-enterologists and general practitioners is urged. A new and more descriptive name, namely, "subacute recurrent duodenitis," is suggested. A series of cases illustrating the roentgenologic findings and symptomatology, are given, the former manifesting themselves in duodenal irritability and hypermotility, indistinctness and haziness of the duodenal bulb, and various spastic phenomena which are inconstant, unlike those seen in duodenal ulcer. The stomach frequently displays signs of irritability and at times definite signs of organic changes. The typical duodenal ulcer syndrome is frequently observed in the symptomatology of duodenitis, making the two conditions indistinguishable clinically. More recent cases of duodenitis display a symptom complex which is rather vague in nature, such as epigastric distress after meals, bloating, belching, nausea, and various neurotic manifestations. Etiologic factors which are responsible in the production of duodenal ulcers are probably operative in duodenitis. Dietary indiscretions and overeating, however, seem to play prominent rôles. The treatment of duodenitis is briefly outlined, consisting of the proper diet, alkalis, anti-spasmodics and sedatives, and medicated trans-duodenal irrigations in selected cases. Suspicious foci of infection should be eradicated.

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Medicine

HEREDITARY EPISTAXIS;
WITH AND WITHOUT HEREDITARY (FAMILIAL)
MULTIPLE HEMORRHAGIC TELANGIECTASIA
(OSLER'S DISEASE)*

(CONTINUED FROM VOLUME II, 40TH SERIES, JUNE, 1930)

By HYMAN I. GOLDSTEIN, M.D.
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During the past twenty-one years I have met with three families in whom epistaxis occurred repeatedly and profusely. The first family (W.) was a typical instance of multiple hemorrhagic hereditary telangiectasia with familial epistaxis. Eleven members of this family were so affected. This family was reported by me in 1921 (*Arch. Int. Med.*).

CASE REPORTS

Recently, one of the patients was treated in the Atlantic City Hospital. In 1918, at the age of forty-two, she had a "stroke," due to bleeding from a cerebral telangiectatic lesion. Blood Wassermann tests were negative. Renal function tests, blood chemistry, blood-platelets, coagulation and bleeding time, and blood-pressure, at that time, were normal. There was no evidence of embolism, hemophilia, purpura, arteriosclerosis, hypertension, endarteritis obliterans, syphilis, uremia, or vascular crises. During her recent stay (April, 1930) in the Atlantic City Hospital, in the service of Doctor Barbash, her condition was very poor, and blood transfusion was necessary. Laboratory studies, made at the hospital, showed as follows:

BLOOD COUNTS

April 3, 1930:

Red blood cells	1,410,000	Large amount anisocytosis, macro-
White blood cells	12,750	cytes predominate; slight poikilo-
Hemoglobin	35%	cytosis; marked achromia and
Color index	1.2+	polychromasia.
Polymorphonuclears	89%	
Small lymphocytes	9%	
Large lymphocytes	1%	
Basophiles	1%	

*Read at the 164th Annual Meeting, June 13th, 1930, Medical Society of the State of New Jersey, Atlantic City, N. J.

April 7, 1930: (After transfusion)

Red blood cells............	1,910,000	Slight poikilocytosis; marked aniso-
White blood cells..........	22,750	cytosis, macrocytes predominate.
Hemoglobin...............	35%	Marked achromia and polychro-
Color index..............	.9+	masia. Occasional nucleated red cell.
Polymorphonuclears........	85%	
Small lymphocytes.........	13%	
Basophiles	1%	
Mononuclear..............	1%	

April 10, 1930:

Differential omitted........   Marked anisocytosis, macrocytes predominate; marked poikilocytosis; marked achromia and polychromasia; slight stippling; occasional nucleated red cell.

April 14, 1930:

Red blood cells............	1,900,000
White blood cells..........	12,500
Hemoglobin...............	30%
Color index..............	.7+

April 15, 1930:

Red blood cells............	1,690,000
Hemoglobin...............	25%

April 16, 1930:

Red blood cells............	2,010,000
White blood cells..........	8,300
Hemoglobin...............	20%
Color index..............	.5

April 22, 1930:

Red blood cells............	1,560,000	Marked anisocytosis, macrocytes pre-
White blood cells..........	6,500	dominate; moderate poikilocytosis;
Hemoglobin...............	10%	marked polychromasia and achro-
Polymorphonuclears........	60%	mia.
Small lymphocytes.........	38%	
Large lymphocytes.........	2%	

Wassermann and Kahn—negative.

April 7, 1930:

Reticulocyte count.........   1.2% Coagulation time, five minutes. Icterus index 2.

April 10, 1930:

Reticulocyte count.........   0.8%

April 14, 1930:

Reticulocyte count.........   1.2%

April 15, 1930:

Platelet count.............   66,000

FIG. 2.

Section through small angiomatous (telangiectatic) lesion *x*.—Epiderm~corium junction.

April 16, 1930:

Percentage of banded white blood cells...............	16%
Blood calcium.............	8.4 milligrams %
Fragility test—	
Minimal hemolysis.......	.40%
Maximal hemolysis.......	.34%

REPORT OF AUTHOR'S CASES

First Family (1918–1921)

CASE 1.—Mrs. R. W., aged forty-two years, white, married, has had severe, persistent and recurring attacks of epistaxis since childhood. She has two daughters and two sons. One daughter, aged twenty years, has bled from early childhood. The other daughter, aged eleven years, has bled from the nose nearly all her life. The patient has telangiectatic lesions on the nose, nasal septum, lips, tongue, chin and cheek. There are a few lesions on the left side of the neck, and one on the middle finger of the left hand. None are seen on the thighs and legs. The larger spots on the tip of the tongue have bled on several occasions. Bleeding from lower lip occurred on one occasion. Sometimes the hemorrhages from the nose are very profuse and uncontrollable. (Frontispiece, Fig. 1, and Fig. 2.) The patient received ferrous carbonate, sodium arsenate, calcium lactate and calcium chlorid at various times. She also used thyroid and lutein for a brief period. Secondary anemia is present. Her eldest daughter has a few spots on the tongue and one over the right clavicle and some on the forearms. The younger daughter has none on the face or body, and only two very small ones are seen on the tongue. The patient's mother, who is dead, also had recurring attacks of epistaxis and red spots. Three sisters are married. Two sisters have nose-bleed; one sister, thirty-four years of age, bleeds profusely from the nose.

Her four children, J. H., thirteen, A. H., eleven, M. H., six, and I. H., three, all suffer from epistaxis. Another sister, A. L., aged thirty-two years, bleeds from the nose. Her son, M. L., aged eight years, does not bleed. A third sister, Mrs. M. C. aged thirty years, and two children, J. C., aged ten years and E. C., aged five years, apparently do not bleed.

Mrs. R. W. (the oldest daughter) had a "stroke" and hemiplegia January 20, 1918, after a little giddy spell. This attack was due to defects in the small vessels, like those occurring in other parts of the body, or a peripheral sclerosis. Blood Wassermann tests were negative on several occasions. Blood chemical tests showed urea nitrogen eighteen milligrams in 100 cubic centimetres of blood; non-protein nitrogen, thirty-five milligrams; creatinin, 2.20 milligrams.

Urine.—January 26, 1918: Trace of albumin; sugar less than 0.1 per cent.; chlorids, 0.5 per cent.; specific gravity, 1.005; granular and hyalin casts; flat and round and caudate epithelial cells; urea, 1 per cent.; acid.

March 11, 1919: Albumin present; urea, 0.5 per cent.; amorphous urates present; total solids, 16.3 grams; faintly acid; specific gravity, 1.009; no casts; no sugar.

July 24: Acid; specific gravity, 1.015; no acetone; no diacetic acid; slight excess of indican fifteen times normal; urea, 0.6 per cent.; no diazo reaction;

slight excess of urorosein; no casts and no cylindroids; many red blood-cells; many renal epithelial cells; large number of leukocytes (pus). Thirty-five ounces of urine were voided in twelve hours.

Eyes.—April 30, 1919: Posterior polar cataracts in both eyes.

*Blood.—*Coagulation and bleeding time normal.

February 15, 1918: Erythrocytes, 3,980,000; leukocytes, 12,600; hemoglobin, 61 per cent. Differential count: polymorphonuclears, 64 per cent.; transitionals, 2 per cent.; eosinophils, 3 per cent.; mast cells, 1 per cent.

July 24, 1919: Erythrocytes, 300,000; leukocytes, 14,600; hemoglobin, 68 per cent.; polymorphonuclears, 60 per cent.; large mononuclears, 12 per cent.; small mononuclears, 24 per cent.; transitions, 2 per cent.; eosinophils, 2 per cent.

The phenolsulphonephthalein renal function test was practically normal. The blood-pressure varied during the past three years between 128 systolic and 90 diastolic, and 110 systolic and 80 diastolic.

*Comment.—*At the time she had the stroke, it was difficult to decide as to the cause. One could not easily differentiate between embolism, thrombosis and hemorrhage. There was no evident source of an embolus. A faint murmur could be heard over the heart, and at times it was faintly audible at the apex, but it could be attributed to the anemia. Shortly after the cerebral hemorrhage, the systolic blood-pressure was 140; however, at no time during the past three years has it been higher than the normal average, often below. She complains of a heavy feeling and numbness in the limbs, and "heaviness with giddy or dizzy feeling in the head." She has crying spells occasionally, worrying over her condition. She was seen by Dr. O. H. Perry Pepper at my request, who reported also that her clotting and bleeding time was normal.

There is no history of hemophilia in the family and none of the family bleed excessively from cuts. One son, A. W., aged twelve years, has several small telangiectases, and a large, pale, reddish nevus on the back of the left shoulder and one telangiectatic lesion below the right lower eyelid. He does not bleed from the nose. The eldest son, L. W., aged twenty-three years, apparently has neither epistaxis nor many telangiectases. There are a few over the scapular regions (supraspinous), and one lesion about four inches below and to the left of the left nipple.

At the time of the "stroke" and since, the patient, Mrs. R. W., has been seen by A. E. Roussel, F. X. Dercum, Charles Potts, W. G. Spiller; A. Gordon, of Philadelphia; T. D. Taggart, of Atlantic City, N. J.; S. S. Butler, of Camden, N. J., and others, during the past three years; however, none of them made the diagnosis of hereditary telangiectasia with recurring hemorrhages, and did not associate the nosebleed and the cerebral complications with the hereditary weakness of the vascular system. Dr. O. H. P. Pepper agreed with me in my diagnosis.

CASE 2.—Mrs. Anna L., aged thirty-two years, married seven years, had one miscarriage at six months, and one premature birth at eight months, the child living only twenty-four hours. Her husband had a positive Wassermann test. The patient had a positive Wassermann nine years ago. She has one boy, M. L., aged seven years, living and well. The boy does not bleed from the nose. The patient has had nosebleed since early childhood, very frequent;

bleeding stops of itself. Had influenza and pneumonia and measles. She bleeds very profusely from the left nostril. Her hands are cold, and she gets short of breath on exertion. Occasionally, she bleeds from hemorrhoids. She has seven or eight small spots over the back, on the shoulders, two small spots back of the ears, several on the left side (anteriorly) of septum of nose and one or two on right side of septum. There are a few radiating dilated capillaries around the alae of the nose. She also has clubbed fingers; these are cyanosed and cold; the lips are cyanosed and get "blue" very often. Blood-pressure: systolic, 95; diastolic, 70. No cardiac murmurs were heard at time of the examination, but the heart sounds were not of good quality; they were weak and muffled. She is a sister of the above patient of Case 1, Mrs. R. W., and to Mrs. E. H. (Case 3). Numerous Wassermann tests have been negative, following specific treatment taken up to a few years ago.

CASE 3.—Mrs. Elizabeth H., aged thirty-five years, has four children. She had one miscarriage. One infant, aged one month, died of whooping cough. She was operated on four years ago for ruptured gastric ulcer with intestinal obstruction. She has been bleeding from the nose almost daily since childhood. She says her mother bled "terribly" from the nose for a great many years, and she thinks her death was due to these severe nasal hemorrhages. She has a pin-point lesion above the right eyebrow; three or four spots on the right cheek over the malar bone; one pin-point lesion on the left cheek, one inch to the left of the outer angle of the left eye; three or four lesions on right half of the lower lip; one spot on the under surface of the upper lip; one on upper gum; one spot on neck at base (right side). She gets attacks of nosebleeding even during her sleep.

CASE 4.—Marvin H., aged five years, was always well, except for severe nasal hemorrhages. He has had nosebleed daily, and during sleep, since he was two years of age. He has one spot on left cheek, one inch below outer angle of left eye, and one on right cheek, one inch below and in front of right ear. Several dilated capillaries are noted on right side of septum of nose. He had measles. Mother says boy "bleeds in streams from nose" daily, which stops itself, after bleeding for five or six minutes. In these cases epistaxis was the first manifestation of the disease. While the hemorrhages have been severe and prolonged, there is only a comparatively mild secondary anemia. In appearance the patients do not look very anemic at all. Sometimes washing the face, or using a handkerchief, or other very slight trauma is sufficient to bring on an attack of epistaxis.

Blood examination.—October 11, 1920: Hemoglobin, 70 per cent.; erythrocytes 2,900,000; leukocytes, 8,000. Differential count: polymorphonuclears, 51 per cent.; small lymphocytes, 45 per cent.; large mononuclears, 3 per cent.; eosinophils, 1 per cent. Marked poikilocytosis. Blood Wassermann, negative.

CASES 5 AND 6.—Aaron H., aged eleven years, and Jeannette H., aged thirteen years, bleed very profusely from the nose since they were two years of age. They are the children of E. H. They have "spots."

Blood examination.—October 11, 1920: (a) Jeannette H.: hemoglobin, 75 per cent.; erythrocytes, 3,350,000; leukocytes, 7,400. Differential count: polymorphonuclears, 72 per cent.; small mononuclears, 25 per cent.; large mononuclears, 2 per cent.; eosinophils, 1 per cent. Some anisocytosis and poikilocytosis.

Blood Wassermann, negative. (b) Aaron H.: hemoglobin, 80 per cent.; erythrocytes, 3,250,000; leukocytes, 11,000. Differential count: polymorphonuclears, 61 per cent.; small mononuclears, 36 per cent.; large mononuclears, 2 per cent.; eosinophils, 1 per cent. Some poikilocytosis and anisocytosis. Blood Wassermann, negative.

	Boggs	Test Tube
Marvin H.	5 minutes	6 minutes
Jeannette H.	6 minutes	7 minutes
Aaron H.	5 minutes	4 minutes

Second Family (1922)

Case 1.—Mr. C., aged thirty-three years, white, adult, male. Auto-parts machinist. Past history negative, except that he has had frequent attacks of nosebleed for many years. In the past three or four years he has been complaining of severe headaches, particularly a left hemicrania.. He is married, has four children, two boys and two girls. His wife has not had any miscarriages. Venereal disease denied. One son and one daughter have had repeated attacks of nosebleed for a number of years. General examination negative. The X-ray findings are as follows:

Teeth.—Periapical abscess at the root of the last upper left molar. This should be extracted. An incipient abscess at the root of the last molar (lower left). This tooth, I believe, can be saved by early instituted treatment.

Sinuses.—Distinct clouding of the left antrum and the right frontal sinuses This condition is due to the presence of a fluid exudate or pus. The other accessory sinuses are normal.

Nose and throat examination showed free discharge of a muco-purulent nature from the left nostril and a degenerated middle turbinate of a colloidal character with obstruction to free drainage from the ethmoid and frontal sinuses. There is distinct evidence of a frontal sinusitis and disease of the left antrum of Highmore.

Case 2.—Dorothea C., aged eight years. White girl, daughter of the above patient. Has had measles, chicken-pox and whooping cough. Has enlarged tonsils and adenoids. General examination negative. Has had repeated attacks of epistaxis and more often than her little brother. On examination, thirty-seven small *brownish spots* were found scattered over the. trunk, neck and legs. One small telangiectatic spot about two inches below the right ear on the side of the neck and the left ear. Numerous very fine and dilated capillaries (arborescent and spider-like) over both cheeks. A few dilated capillaries are seen over the left nasal ala. One dilated capillary visible over the sternal end of the right clavicle and one over the right shoulder. There are some visible capillaries over the space between the left scapular spine and vertebrae.

Case 3.—Harry C., aged six years. White boy, brother to the above patient. Has had measles, chicken-pox, la grippe, and whooping cough. Has attacks of hemorrhage from the nose. These attacks are not very frequent of late. General examination negative. Has a pale pink nevus on the back of the neck, two inches by one-twelfth inches. Has another "birth-mark". over the

middle of the back one and one-quarter by three-quarter inches. He has twenty-eight brownish spots scattered over the body, resembling dark pigmented freckles. There is visible one area of dilated capillaries over the left cheek. The father had several telangiectatic lesions, one or two on the neck and about thirty-five or forty dark pigmented spots, dark brown in color, scattered over the neck, trunk and arms. His tonsils were removed about eight months ago.

Third Family (1929)

Mr. H., aged twenty-nine years. Suffering from migraine and headaches for past fifteen years. Had diphtheria, typhoid fever, pneumonia, three attacks of acute articular rheumatism. Now has occasional pains in the joints. Had nosebleed frequently and nearly bled to death following tonsillectomy. Is "drowsy" and "fatigued" and cannot concentrate. Mother has diabetes. Father and two brothers had nosebleed. Blood Wassermann tests were negative. Urine analysis, negative. Bleeding time, two and one-half minutes. Clotting time, eleven minutes (hypocalcemia). Blood calcium, 7.9 milligrams per 100 cubic centimeters blood. Blood sugar, 90 milligrams per 100 cubic centimeters blood. Blood count, red blood cells, 4,390,000; blood-platelets, 290,000; white blood cells, 10,000.

Differential: Polymorphonuclears, 59 per cent.; small lymphocytes, 39 per cent.; large lymphocytes, 1 per cent; basophils, 1.

X-ray of sinuses: Clouding of left antrum. Sella turcica, normal. *Teeth*: negative.

Eye examination: Low amount of far-sighted astigmatism.

Basal metabolism: minus 25 per cent.

Removal of the tonsil stump, cleaning the antrum, the administration of thyroid extract, calcium, parathormone, and ultra-violet ray therapy brought about rapid improvement.

The blood calcium rose to eleven milligrams; blood uric acid, 3.8 milligrams; creatinine, 1.4 milligram.

The basal metabolism became normal. One brother, aged twenty-three years, bled severely after tonsillectomy. Bled from the nose occasionally. Another brother, aged twenty-five years, bled profusely after tonsillectomy (1924), followed by pneumonia. Bled from the nose. Another brother, aged forty-two years, used to bleed from the nose. His three sons do not bleed. The father, aged sixty-eight years, had severe nosebleeds, when younger. One sister and one brother do not have nosebleed.

These instances of familial epistaxis resemble the type of cases reported by Giffin, of the Mayo Clinic, in the *American Journal of Medical Sciences*, 1927.

DIAGNOSIS

The differential diagnosis must be made from "pseudo-hemophilia," hypertensive epistaxis, purpura hemorrhagica, hemophilia, pernicious anemia, tuberculosis, deficiency disease, or "hemorrhagic diathesis." Blood-platelets, bleeding and clotting time are usually

normal. Men and women are affected, and both sexes may transmit the condition.

As the condition is due to some hereditary defect of the vascular system, little can be done.

For the local bleeding, the chromic acid bead, electric cautery, carbon-dioxid snow, astringents, and radium have been tried. The administration of calcium by mouth and intravenously, parathormone injections, viosterol, ultra-violet ray and X-ray therapy, liver liver-fraction, iron, arsenic, and endocrine therapy have given varying results. In severe hemorrhages, whole-blood injections, blood serum, blood transfusion, coagulen, claudel, stryphnon (Meyer and Albrecht), thrombo-plastin, afenil (intravenously) and calcium gluconate may be useful.

Professor B. Niekau (Tübingen) and Professor F. Llopis (Madrid), recommend the use of Nateina Llopise, a preparation of a mixture of vitamins A, B, C and D, of vegetable origin, to which calcium phosphate and lactose have been added. Five tablets are chewed on an empty stomach, before meals. This is considered a good remedy in hemophilia.

Taylor (July, 1929), has apparently cured purpura hemorrhagica by the use of *bothropic antivenin.*

Rendu suggests cold compresses to the head and neck, lifting the arms, decoction of walnut leaves, or a little alum, tamponing when necessary, and the administration of opium. Gubler believes opium is the best remedy in some cases when epistaxis is excited by excessive nerve stimulus.

Pagueguy (Paris, 1831), recommends the introduction of a piece of hog's intestine prepared in the form of the finger of a glove, and this can be filled with fluid by means of syringe after which a ligature is applied to prevent the escape of the fluid. Thus the mucous membrane of the nose is compressed and the hemorrhage arrested. Wicks of lint moistened with alum solution were used for tamponing. He used wine of quinin and iron as tonics.

Gjessing uses calcium lactate regularly and as a prophylactic remedy.

Osler uses calcium chlorid.

Emile-Weil suggests using carbon-dioxid snow (June, 1926), and has obtained some good results.

Leeches applied to the back of the neck and to the buttock were advised by Sacharin, of Russia.

Compression of the nose with thumb and index finger is at times a useful procedure.

Stenger (1915), in his Thesis for the University of Wurzburg, discusses, most thoroughly, the various forms of treatment for nasal hemorrhages. He suggests the use of cauterization with chromic acid crystals or silver nitrate for the telangiectases, followed by loose tamponage with 10 per cent. bismuth ointment. He has also tried styptol, secacornin, coagulen and the gelatins.

McBride (*University of Penna. Med. Mag.*, vol. 2, pp. 424–426, 1889–1890) reports two fatal cases of nosebleed and one case that was nearly fatal. This patient was a law student, aged seventeen, who bled for many days. D. Hayes Agnew suggested two cylinders of bacon so as to tightly plug the nostrils. This stopped the bleeding for a while. Later, McBride used a cylinder of ham fat which "acted like a charm." Edward Martin and the late J. William White, of the University of Pennsylvania, also saw this patient.

Angioxyl may be used by injections and by mouth, in the hypertensive and arteriosclerotic cases (with iodides).

I wish to emphasize only two things: First, *the differential diagnosis* must, of course, be made from pernicious anemia, severe septic infections complicated by petechiae and hemorrhages, hemophilia, so-called pseudo-hempohilia, various deficiency diseases, purpura hemorrhagica, leukemias and anemias, simple telangiectases and hypertensive and arteriosclerotic hemorrhages and gastro-intestinal and nasal bleeding due to other evident pathologic conditions. Parkes Weber of London (Brit. Journ. Derm. & Syph., Aug. 1930) discusses "Telangiectasia macularis eruptiva perstans" and alludes to familial hemorrhagic cases. He agrees with me that Curschmann's cases were really not hemophilia at all but instances of "Rendu-Osler-Weber's Disease." Remember, if you please, that in this interesting clinical entity both sexes are equally affected, and both male and female may transmit the condition. Blood pictures, with the exception of secondary anemia, are usually normal. Blood platelets and bleeding time are normal. Hemorrhages may occur

from the stomach, the bowels, the rectum, the bronchi, and we may even meet with hemorrhages into the eye and from the tongue, gums and lips. In one of my cases, hemorrhage occured from telangiectatic lesion under the fingernail, and from the tip of the tongue. Hematuria may be met with in these cases.

Second, as to *treatment*, which I did not not dare to discuss fully in the original paper in the presence of such distinguished otolaryngologists. My good friends Drs. Barkhorn and Ersner have covered this part of the subject most admirably. I may' add, however, that Professors Agnew and Martin of the University of Pennsylvania used bacon packed into the nose to stop nosebleed when other measures have failed (1865 or 1870). Later, McBride, treating a law student from the University, seventeen years of age, used ham fat to stop the bleeding when everything else failed. Nasal bleeding was also stopped by the use of hog's intestine inserted in the nose, filled with fluid and tied. More practical measures, however, in cases of this disease, to stop the hemorrhages are the *cautery* for the local approachable lesions, *x-ray* over the spleen, *clauden* (Luitpold-Werk, Munchen) by injections and tablets by mouth. It is also obtainable in powder form. *Stryphnon* ("Phiag," Vienna) is very effectual given intramuscularly or intravenously, and used also in powder form locally. Intravenously one may use *afenil* (10 cubic centimeters—10 per cent.), calcium gluconate ("Sandoz"), gulen ("Ciba"), and gluco-calcium ("Lilly"). Whole blood injections, blood transfusion, thromboplastin, kephalin, parathormone (by injection); calcium lactate, calcium chloride, kalzan, calcium gluconate by mouth have all been used with' more or less effective results. Mesothorium has been used with some effect. In the hypertensive arteriose¹ ᵗⁱᶜ cases with hemorrhage that may occur in some member of   ᵗⁱᵉs as in others, not affected with Osler's disease,—the us⸱   ᵥremedies is of course indicated. In such cases iodid⸱   injections of *angioxyl*, 20 to 40 hypotensive unit   as necessary. Angioxyl was intro⸱⸱ed ᵗⁱr   onths by Professor Henri Vaq⸱   his ⸱   is a de-insulinized pancreai ⸱ ⸱   ᵘⁱs preparation may be ⸱ᵥ⸱   ᵥ⸱ ⸱ or angioxyl.

CONCLUSIONS

1. A review of the literature of the world on the subject of familial epistaxis and hereditary telangiectasia is here briefly discussed.

2. There are probably a total of sixty-five families and about 350 individuals suffering with this clinical entity—"hereditary (familial) epistaxis with multiple hemorrhagic hereditary telangiectasia" —on record in the entire available medical literature of the world.

3. Many cases, no doubt, have been overlooked by the otolaryngologist, dermatogolist, and pediatrician. A more careful study of cases of epistaxis and of those complaining of various forms of telangiectases and angiomatous lesions of the skin and mucous membranes will bring to light additional cases of this disease entity.

4. Cases of *familial* hematuria, hemorrhagic nephritis, hemoptysis, "gastrostaxis," intestinal and gastric bleeding, and some of the so-called essential idiopathic hemorrhages are probably different forms of this disease.

5. Reports of cases of familial epistaxis, with and without skin and mucous membrane (vascular) lesions, are included in this paper.

[NOTE.—An elaborate bibliography for the research scholar may be obtained as long as the supply lasts by application to the AUTHOR or to EDITOR of the CLINICS, Box 311, Burlington, New Jersey.]

from the stomach, the bowels, the rectum, the bronchi, and we may even meet with hemorrhages into the eye and from the tongue, gums and lips. In one of my cases, hemorrhage occured from telangiectatic lesion under the fingernail, and from the tip of the tongue. Hematuria may be met with in these cases.

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Medical Questionnaires

Collated by B. BICKEL, M.D.

Washington, D. C.

What has been found out regarding "ginger paralysis"?

In spring, a number of patients with flaccid paralysis starting with soreness of the calves of the legs, and inability to control the movements of the feet, applied at the East Mississippi State Hospital for sweat baths. Some were compelled to use sticks and crutches to move about. Many cases have been seen since in the South and some elsewhere. The nature of the malady is still not well explained, but most patients had been using alcohol, or rather, so-called "Jakey," a Jamaica ginger adulteration. The paralysis resembled Landry's. This beverage has always been widely used, but it is not until recently that severe damage has resulted. Among fifteen cases treated at Boston City Hospital between March 4 and 28 of this year were only two without a history of alcoholism, and most of them had partaken of ginger extract for years. One patient had taken five bottles of two-ounce content within three days as a recuperant from influenza.—Trophic disturbances are rare, and, if present, are mild. Often the upper extremities become involved. The skin on the feet becomes shiny. There may be difficulty in passing urine, and steppage gait and drop-foot are not uncommon. Pain is not severe, but there is numbness.—With coöperation of the Prohibition Bureau, the Hygienic Laboratory, after collecting samples, especially from the southern states, has carried on investigations regarding the actual cause of this type of paralysis. The destillate, upon saponification and subsequent acidification, gave a positive reaction for phenols, while unsuspected unadulterated gingers and U. S. P. fluid extract of ginger did not have such reaction. Rabbits which received such adulterated ginger died from respiratory paralysis preceded by symptoms resembling those of phenol poisoning. Monkeys and dogs suffered no bad effects from any of the gingers, including the adulterated.—Jeter performed an autopsy on a man

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who died in an attack of this kind of paralysis. He believes that the old man died of cerebral edema, precipitated by renal congestion. Senility and chronic alcoholism were evidenced in interstitial changes.—The treatment recommended by Seale Harris is a diet rich in the antineurotic vitamin B, whole-wheat bread, cereals, citrus fruits, leafy green vegetables. Constipation must be combated. During the chronic stage galvanic stimulation of the nerves is suggested.

BENNETT, C. R.: "A Group of Patients Suffering from Paralysis Due to Drinking Jamaica Ginger," *Southern Med. J.*, vol. 23, pp. 371–380, 1930.

HARRIS, SEALE: "Jamaica Ginger Paralysis," *Southern Med. J.*, vol. 23, pp. 375–380, 1930.

JETER, HUGH: "Autopsy Report of a Case of So-called Jake Paralysis," *J.A.M.A.*, vol. 95, pp. 112–113, 1930.

MERRIT, HOUSTON AND MOORE, MERRILL: "Peripheral Neuritis Associated with Ginger Extract Ingestion," *N. Engl. J. of Med.*, vol. 203, pp. 4–11, 1930.

SMITH, M. I., ELVOVE, E., etc.: "Pharmacological and Chemical Studies of the Cause of So-called Ginger Paralysis," *Publ. Health Rep.*, p. 1703, July 25, 1930.

Is the temperature of fluids drunk indifferent for elimination?

Basch and Meutner find that diuresis is more marked from fluids taken at 40°C. than at 10°C. Cold drinks are more slowly eliminated than those of body temperature. So, hot milk for sweating still is in order and we will tolerate heat better for the cold drink which is willing to act longer for our relief.

BASCH, FELIX, AND MEUTNER, HANS: "Der Einfluss der Temperatur getrunkener Flüssigkeiten auf die Verweildauer im Magen und die Ausscheidung durch die Niere," *Klin. Wchnschr.*, vol. 9, pp. 1258–1259, 1930.

What do club fingers indicate?

Josefson found that aneurysm of the subclavian artery produced, or was associated with, club fingers. The hand of the same side is the one involved, often only one of its fingers. Where it was found in both hands the aneurysm was apt to be bilateral. In one instance the author disclosed a syphilitic infection which the patient himself did not suspect. The club fingers led to a Wassermann test.

JOSEFSON, A.: "Fall med Förstoring av ena Handens Fingrar pa Grund av Aneurysma i Arteria subclavia," *Svenska Läkartidningen*, vol. 27, pp. 937–942, 1930.

What results from one-sided egg diet?

Friedberg and Abraham investigated the effect of whole egg, white of egg and yolk, raw, soft-boiled and boiled twenty minutes, on rats and mice. The white of eggs alone is not sufficient food for rats, as not enough can be taken to cover the necessary calories, and evidently the white is damaging, though the ill effect is somewhat counteracted by heating. However, as more of the heated eggs can be taken than of the raw, the damaging effect remains. If rats are fed total egg exclusively for more than two months they lose weight and show trophic disturbances. They never survive four months of raw or soft-boiled egg feeding, while eggs heated at 100°C. may keep animals alive one year, and no trophic disturbances arise. Feeding the yolk for one year did not have the same trophic effect. A vitamin problem arises here. It is the white of the egg which is not conducive to growth and well being. Eggs in large numbers were prescribed about thirty years ago, a procedure which modern medicine is not willing to adopt, though several eggs are advised with orange and lemon juice, fruit and a little meat by those study-ing caries prevention, more especially by a group of dentists of California. Every now and then some one launches warfare against this food which has weathered many an assault.

ALDRIDGE: "Discovery of the Constant Presence of Grape Sugar in the White of Eggs," *Med. Times*, p. 437, London, 1849.

FRIEDBERG, E., AND ABRAHAM, A.: "Ueber die Folgen langdauernder einseitiger Fütterung mit Eiern," *Ztschr. f. d. ges. exper. Med.*, vol. 77, pp. 490–513, 1930.

ROSEWATER: "Objections to Raw Eggs in Diet," *J.A.M.A.*, vol. 80, p. 302, 1923.

Can a former paralysis be diagnosed, after it has been healed?

Paralysis is not considered inevitably progressive at present. It may be important to learn whether paralysis may be pronounced cured for insurance or legal purposes. Many of the intellectual residual conditions, persisting after treatment of general paralysis with malaria, may be disclosed in the office; much may be gained from the reports made by the patient's family, especially as regards volition and emotional reactions. Pupillary reactions may be re-gained; differences in the size of the pupils will never be overcome. They are signs of destruction, but not of active paralysis; the patient

may be entirely restored mentally. Of course, this symptom, if isolated, does not answer the question. Often the inequality of pupils will be brought out only upon dilatation with atropine, possibly at a casual examination of the eye. Speech defects may cease after successful treatment. Often the patient, especially the intelligent one, may be conscious of this defect, and it may even seem accentuated upon later reëxamination.—If the paralysis is no longer active after treatment, and the patient can be considered well, the cell count and globulin reaction are almost always normal; not quite as regularly, but generally, the cerebrospinal fluid Wassermann reaction is negative and in about 50 per cent. the Wassermann reaction of the blood as well. Among 200 cases of treated paralysis, only one, however, had a fully normal mastic reaction. So, if, after years of reëxamination, the mastic reaction is normal, one may decide that the disease has not existed for the time following the treatment. A wide margin is given, Pönitz postulating six years of such freedom from positive mastic reaction.

PÖNITZ, KARL: "Die Diagnose der abgelaufenen paralytischen Erkrankung," *Deutsch. Ztschr. f. Nervenhlk.*, vol. 114, pp. 104–113, 1930.

Should milk teeth be extracted?

Leist, on the basis of roentgenograms, claims that every extraction of a milk tooth occasions an occlusional or positional anomaly. Clinically, the maladjustment may not be very apparent, but the roentgenogram will reveal it. Caries and faulty position result in the temporary set, and may extend to the permanent. Teeth begin to move together and tilt, and the unerupted, unfinished teeth are displaced. The pictures accompanying Leist's article are very revelatory, showing a mass of unerupted teeth tumbled at all angles. It is necessary to preserve an ungaping line in the child's set of teeth. This is the more important the younger the child. Not infrequently, it was found, a permanent tooth is extracted with the temporary, unawares at least to the patient or his parents. The gap is no longer of adequate size for the later erupting tooth, the direction of the roots is changed by crowding of the neighbors toward the gap.

LEIST, M.: "Weitere Röntgenstudien am kindlichen Gebiss nach Milchextraktionen," *Ztschr. f. Stomatol.*, vol. 28, pp. 543–552, 1930.

Is there finality in the cancer statistics?

Newer cancer statistics, which have been made an international endeavor, are reaching the medical press in great numbers, and it is evident that it will not be possible to understand them until the information gleaned has been summarized by each nation. The greatest problem is the correct appraisal of effect of age groups on the figures.—By 1900, cancer operations were well established, but dependable reports of lasting success were few. This was partly due to the fact that large numbers of cases, which are now considered inoperable, were given surgical treatment in the hope that removal of the main tumor in evidence would arrest the process, and, furthermore, there were the innumerable metastases. Then the five-year cures were taken for granted. Those operated upon before metastases form are the favorable surgical risks.—Cancer is a subject spreading to press-item magnitude, and the public health aspect has reached even to prenatal care; it has made many more people attentive to lumps and bone pain, and other precancerous indications.—Bloodgood believes that the only service that can be rendered as preventive measure is to supply the public with dependable information.— Medical statistics, to counteract error, should be taken from various parts of the world, but must be comparable. Methods have created greater uniformity. The pitfalls are still numerous. Many a practicing physician is loath to attest to death from cancer, especially in the rural districts. Prevention being the goal, figures become distorted.—Germany reports 76,000 deaths from cancer annually. There figures are gained by dividing the number of cancer cases by 10,000 inhabitants. This number is multiplied by 10,000 of the population of the following year, and so arrives at the figure of expected deaths. Deducing this figure from the official cancer figures, the actual increase of cancer mortality is arrived at, while the difference of the official figures of this and the preceding year provides an apparent increase. Under this computation, for instance, Bavaria has an actual increase of 203 cases per year. There was an annual average increase of 138 during the eight years before the war. Age groups were not found responsible. Mertens points out that this increase could not be attributed to better diagnosis, as fluctuations continued even during the years of Roentgen introduc-

tion.—Dunlop argues that it is almost inconceivable that cancer of the breast, for instance, should become fatal without being diagnosed. Cancer of the uterus has decreased, according to international investigations. For the same scope of inquiry on breast cancer among married women the figures differ considerably. Age for age group mortality is higher for breast cancer in unmarried women than for the married. Dunlop believes better diagnostic facilities are the reason for the cancer mortality increase, barring breast cancer. Also to ageing of populations, Dunlop would like to attribute two-thirds of the increase for cancer mortality among the male and four-fifths of the increase among females in the statistics gained for the period of 1911 to 1928.—In Scotland, cancer of the stomach and intestines shows an increase of 13.3 and 21.3 per cent., respectively. The same figures for England are 22.8 and 46.8 per cent. Cancer of the rectum has increased by 17.9 per cent. in England, and 6.7 per cent. in Scotland.—Of 14,264 bodies, of which 1393 were dissected, at the age of fifteen or more, there were 2800 cases of cancer and 630 of sarcoma at the Göttingen pathologic institute between 1921 and 1927. Among the autopsies 203 cases of cancer and twenty-three of sarcoma were found, and thirty-seven of glioma. Among the bodies sent in were 810 male and 1686 female cases with cancer, a relation of 1:2. Among the latter were fourteen, of whom the ages were not given. For those coming to autopsy the relation was reversed; there were 127 male and seventy-six female bodies with cancer, a relation of 1.7:1. Many writers have shown that women get cancer earlier than men. If the genital cancers are barred, gastric cancer predominates, is about equally common in both sexes, and is seen not only in the old, but between the ages of thirty-six and sixty-five. No decrease was found since the war by Egenolf, but an increase in pulmonary and bronchial cancers. These are but a few examples that baffle investigation.

BLOODGOOD, JOSEPH COLT: "Cancer a Public Health Problem," *Clin. Med. and Surg.*, vol. 37, pp. 187–191, 1930.

EDITORIAL: "The Increase of Mortality from Cancer," *Brit. M. J.*, No. 3628, p. 109, 1930.

EGENOLF, WILHELM: "Ueber die in den Jahre 1921–1927 vom Göttinger Pathol. Instit., beobachteten bösartigen Geschwülste," *Ztschr. f. Krebsforsch.*, vol. 31, pp. 396–431, 1930.

MERTENS, V. E.: "Nimmt der Krebs in Bayern zu?" *München. med. Wchnschr.*, vol. 77, pp. 1227–1228, 1930.

What are some of the clinical applications of studies on constitution?

The most quoted constitutional make-up is that of the tuberculous, more especially the thorax of those who contract the disease. However, there are too many suffering from the malady to be confined to one type entirely. Recent studies of Eugen Schlesinger on children and juveniles have shown that the leptosome type is more disposed to constitutional anomalies than the pyknic. This applies to neuropathies and residues of exudative diathesis and of postural anomalies, manifesting themselves in constitutional muscular weakness. The broad pyknic are the physical superiors to the middle-sized muscular, and they, in turn, to the slender leptosomes. In them a higher proportional thoracic circumference produced a more favorable proportion of the thorax in the pyknic, and better proportions of body weight and height. The pyknic are rarely retarded or undernourished. Naturally, these results are useful for average rather than for individual evaluation. In later age groups the conditions may change. The study shows that slenderness is not the most favorable aim. This does not take the dangers from internal organs into consideration. Yet the pyknic generally are less liable to contract the diseases of childhood, always sensible hygienic conditions being equal. The general practitioner learns which of his patients are poor risks, especially those who have a larger practice of people who come for examinations for insurance purposes, and if he stays long in a certain community whose population happens not to change too often, he knows his family types, and will be able to warn those who are most likely to contract certain diseases, if they will only let him. The time of monosymptomatic medicine, as Kraus calls it, is yielding to conceptions of syndromes, blood types, and diatheses. Functional or morphologic conditions are made the center of attention. Function and form must be considered together. They are bound together like cause and effect. Constitution is the center of present-day case taking. Even ageing is at last not being taken symptomatically; and, in fact, it is an harmonious procedure, in which the individual body constituents and parts age one with the other, depending upon constitution and type. Schlomka points out that it is not the testicles which start, the other

organs following, at least where matters proceed according to physiologic laws. Such heterochronic ageing, he believes, may be influenced to a certain extent by remedies. Arteriosclerosis, he shows, is a physiologic ageing of the aortic wall.—By the way, Marg. Hesse and K. Wolkoff found considerable resemblance in arteriosclerosis of parrots when comparing it with that of man. They find that it increases gradually with age, and that it is not bound to increased intake of cholesterine or especially lipoid containing food, as was seen in the rabbit by other laboratorians.—In the field of obstetrics Zondek distinguishes between fat and not fat amenorrhea. A female constitution should be fully developed and have normal menstruation and fertility. All types in gliding scale are found in the genital function, normal physical constitution with disturbances in the cyclic function (or fertility), or faulty physical constitution with normal cyclic function (or fertility). Certain menstrual forms are typical of certain physical builds. For ovarian insufficiency and hyperplasia of the body, Glasmer finds lipoid-soluble substances indicated and water-soluble ones in the same insufficiency of hypoplasia. The hormone therapy needs closer study, in connection with the constitutional requirements. Bleeding at puberty was found to improve under cholin administration, and it was useful for climacteric hemorrhage. Cycle hormone preparations should be developed.

HESSE, MARG., AND WOLKOFF, KAPITOL: "Ein Beitrag zur Kenntnis der Atherosklerose," *Centralbl. f. allg. Pathol. u. pathol. Anatom.*, vol. 49, pp. 40–46, 1930.

GLASMER, ERNA: "Ueber die Notwendigkeit einer Neuorientierung der endokrinologischen Symptomatologie. Zugleich ein Beitrag zur Konstitutionstherapie des Weibes," *Ztschr. f. Geburtsh. u. Gynaek.*, vol. 98, pp. 105–123, 1930.

SCHLESINGER, EUGEN: "Die Ueberlegenheit der Breitgebauten über sie Schlanken," *München. med. Wchnschr.*, vol. 77, pp. 1090–1093, 1930.

SCHLOMKA, G.: "Uebers neuere Ergebnisse der Altersphysiologie," *Med. Klin.*, vol. 27, pp. 1065–1070, 1930.

What are etiologists saying about psittacosis?

The impression, mainly of European medical writers, is that the Nocard bacillus is not the pathologic agent of psittacosis. However, both Clementi and Bermann of Cordoba have found this microorganism in birds at the time of an epidemic among parrots at an exhibition of these birds first at Cordoba in Argentina, and again

after the entire show was removed to Tucuman. Many of the dealers took the infection, which appeared much like influenza at the time, with 25 per cent. mortality. The European and many of the North American investigators found streptococcus, and concluded that it is a mixed infection in man, the streptococcus helping to make the pathologic agent noxious. Nocard bacillus was not found by them, but a filtrable virus which proved fatal upon inoculation into other parrots. The question arises whether the microörganism had reached a different cycle by the time it had been transported overseas. Not the same family of parrots was used for all experiments. Adamy incriminates the Brazilian green Amazone parrot, Kurikki (Chrysotis amazonica). Herderschêe, of Amsterdam, found non-hemolytic streptoccoci and gram-positive diplococci and rods. Volterra and some other writers speak of transmission to humans from parrots which have recently been imported from Brazil—in his case—to Florence, stressing the recent arrival. Lillie found rickettsia-like inclusions in man and experiment animals at autopsy. In the livers of both man and animals he found cellular inclusions of small gram-negative cocci and bi-polar formations of about 0.2μ to 0.3μ in reticulo-endothelial and mesothelial cells, and large mononuclear cells in the parrot and in man. He suggests the name of rickettsia, which, however, he does not name as the microbacillus of psittacosis. Armstrong and McCoy succeeded in inoculating parrots with a filtrable virus of the internal organs of a parrot which had died of inoculation psittacosis. Volterra names some of the paratyphoid B enteritis group as "virus de sortie." This writer believes that for man, a certain exhaustion or old age is necessary to render the case fatal. Coles saw a lot of organisms in the smears of blood from heart, spleen, and other organs in hens inoculated with psittacosis. There were small diplococcoid bodies and single small bacilli and diplobacilli. The diplococcoid bodies were the most characteristic and stained red with Giemsa dye. Their average diameter was $0.6–1.7\mu$ by $0.3–0.4\mu$. They were thin rods, 0.2μ in diameter, also staining red with Giemsa. Coles believes that the coccoid bodies might possibly be the pathologic agents of psittacosis. Again epidemiology narrows down to bacteriologic search, with the aim of finding the mode of treatment which has, so far, not been very successful.

ADAMY, GUSTAV: "Klinische Erfahrungen über die Papageienkrankheit (Psittakose)," *Deutsch. med. Wchnschr.*, vol. 56, pp. 217–219, 1930.

ARMSTRONG, CHARLES, AND McCOY, G. W.: "Filtrability of the Infective Agent of Psittacosis in Birds," *Publ. Health Rep.*, p. 725, 1930.

BEDSON, S. P., WESTERN, G. T., AND SIMPSON, LEVY, S.: "Further Observations on the Etiology of Psittacosis," *Lancet*, vol. 1, p. 545, 1930.

BERMANN, GREGORI: "Die Psittakose-Frage in der Republik Argentinien," *Med. Welt*, vol. 4, p. 178, 1930.

CLEMENTI: "Papageienkrankheit (Psittakosis)," *Deutsch. tierärztl. Wchnschr.*, vol. 38, p. 40, 1930.

COLES: "Psittacosis." Letter from London, *Deutsch. med. Wchnschr.*, vol. 56, p. 1227, 1930.

ELKELES, G.: "Ueber die Berliner Fälle von Papageienkrankheit und den derzeitigen Stand der Psittakosisforschung," *München. med. Wchnschr.*, vol. 77, pp. 139–140, 1930.

HERDERCHEE, D.: "Gevallen van Psittacosis in Amsterdam," *Ned. Tijdschr. Geneesk.*, vol. 1, p. 873, 1930.

LILLIE, R. D.: "Psittacosis: Rickettsia-like Inclusions in Man and in Experimental Animals," *Publ. Health Rep.*, p. 773, 1930.

REINECK, AND HOFMANN, PAUL: "Bakteriologische Befunde bei Psittakosis," *Deutsch. med. Wchnschr.*, vol. 56, pp. 516–517, 1930.

SIEGMUND, H.: "Zur pathologischen Anatomie der Psittakosis (auf Grund von Untersuchungen während einer Hausepidemie im Sommer 1929)," *München. med. Wchnschr.*, vol. 77, pp. 223–225, 1930.

VOLTERRA, MARIO: "Die Psittakosisepidemie in Florenz, Oct., 1929," *Zentralbl. f. inn. Med.*, vol. 51, p. 545, 1930.

How much does the roentgenogram aid in diagnosis of mastoiditis?

Acute mastoiditis may be considered always secondary to an infection spreading from the middle ear, states Blaubaum. There is, he admits, that arising from an infection of the blood-stream. In acute cases of otitis there is pus in the mastoid antrum, but also infection of the mucous lining of the cavity. Discharge soon ceases when spontaneous rupture of the tympanic membrane occurs. The acellular type of bone may, however, become involved. In the mastoid antrum there is practically only one cell; most of the bone is solid. The inflammation may extend to the zygomatic arch or to the occipital bone, or downward to the mastoid tip. Inflammation spreads from cell to cell easily. The mucous lining swells and pus breaks down the bone trabeculae. The roentgenogram shows blurring of the air spaces in the cells, and thickened trabeculae, or large cells with uneven contours. The ears and adjacent bone structures of

both sides should be examined for comparison.—Fleischmann and his companions were able to demonstrate tumors, pyramidal fractures, pneumatic conditions and acute mastoiditis with swelling of the mucous membranes and accumulation of pus, bone abscess and defects of the mastoid cells, also choleastoma. Hanse has published 500 roentgenograms which reveal mastoid conditions well. Not much information was gained regarding the soft parts. He found that mastoid cells are indicative of chronic conditions. Helwig, and Dixon, incidentally, found that many children with grave digestive disturbances presented signs of mastoiditis. Johnston, Brown and Tiedall state that intestinal intoxication is not due to masked infection in the middle ear or mastoid antra, but is an enteral infection caused, not by one specific bacterial species, but by a variety of bacilli which belong to the colon-typhoid-dysentery group.

ALEXANDER, G.: "Ist es empfehlenswert, die akute Mastoisitis vom äusseren Gehörgang aus zu operieren?" *Monschr. f. Ohrenhlk.*, vol. 64, pp. 792–801, 1930.

BLAUBAUM, ATHOL: "Acute Mastoiditis," *Med. J. of Austral.*, vol. 17, pp. 48–49, 1930.

FLEISCHMANN, LASZLÓ, AND REVESZ, VIDOR: "Die moderne Roentgenuntersuchung des Gehöroganges," *Therapie*, vol. 7, pp. 43–45, Budapest, 1930.

HELWIG, FERDINAND C., AND DIXON, O. JASON: "The Frequency of Mastoiditis in Infants," *Arch. of Otolaryngol.*, vol. 11, pp. 169–177, 1930.

JOHNSTON, MARION M., BROWN, A., AND TIEDALL, F. T.: "Enteral Infections in Acute Intestinal Intoxications," *Canad. Med. Assoc. J.*, vol. 23, pp. 231–237, 1930.

What is common sense in treating wounds?

For all wounds rational stopping of hemorrhage and protecting the lesion from outward influences. The part should be given absolute rest by fixation, to prevent inflammation, and to combat inflammation in inflamed wounds. If the injury comes under treatment within the first six hours, hemorrhage may be stopped by ligation or sutures carried around it; excision of ragged edges and parts which have been cut off from the blood circulation is indicated. Sutures must be strictly aseptic, and the covering dry, air-admitting, and aseptic. Small lacerations and cuts may allow of adapting the edges and using plaster covering. Where any indications exist of injury to joints, tendon or bone, this is the surgeon's territory. Small wounds which cannot be sutured, stabs, shots, etc., are covered.

with dry pressure bandages, hemorrhage stopped or the injury treated with powder which forms a scab, for instance, sodium sozoiodolicum, dermatol, calcium chloride, or bolus alba. There is, of course, danger from infectious matter in such cases, therefore the wound must be examined within forty-eight hours. Severe hemorrhage requires dry antiseptic tampon, pyramidal in form.—After the primary stage of wound healing is passed, or when infected, immobilize and use alcohol bandages.—Inflamed wounds and localized abscesses are treated with the moist chamber or the thermophore.—Granulated wounds are treated with ointment bandages. Hypertrophic granulations and hypersecretion should be treated open.

DEMMER, F.: "Welche Wunden sind trocken, welche feucht und welche mit Salben zu behandeln?" *Mitt. d. Volksgesundh-Amts*, No. 8, pp. 237–239, 1930.

What features have been brought out by recent investigation of rheumatism?

Lindstedt has pointed out that care must be exercised in diagnosing the pain with which the patients present themselves, a very common difficulty. The postural changes resulting from rheumatic or neuralgic conditions lead to pain. In rheumatic cases the muscular pain may be traced in most instances by following the line of extensor action.—A diagnostic feature has been brought out by Dawson, Sia and Boots, who find the sedimentation rate of the red blood-cells greatly increased, as a rule, to about thirty millimeters per hour, or more. In rheumatoid arthritis, it parallels severity and extent of the arthritic process; in old and arrested cases the sedimentation rate tends to return to normal values. In cases of osteoarthritis, values rarely attain more than thirty millimeters. Non-articular rheumatism shows normal, or very slightly elevated sedimentation.—Causes for the many clinical forms of rheumatism continue numerous. Aschner, evidently knowing his Paracelsus, finds that one-third to one-half of all arthritic-neuralgic rheumatism in women presents scant menses; they need have no discoverable purulent or other infectious foci. The conditions prevailing are similar to those found in uric acid diathesis. Weil quotes Hippocrates who saw the rheumatism of two patients relieved by dental cure. Figures for interrelation of teeth and rheumatism given vary

from 35 per cent. to 54 per cent. for rheumatic arthritis and more for osteo-arthritis, and Buckley gives 95 per cent. of dental focal infection. At present these focal infections are believed grossly exaggerated. Removal of tonsils and teeth has not always stopped rheumatism. No results were obtained in chronic polyarthritis. Holstein declares the tonsils of healthy individuals normally harbor slight chronic inflammation. Weil shows that angina precedes in 71.4 per cent. of acute rheumatism, in 47.3 per cent. of recurrent rheumatism and in 22.2 per cent. of chronic rheumatism. Lacunary angina generally persists after the joint has been cured, and rarely is the sequence reversed. Weil believes there is no causal relation, and that purulent tonsillitis is but a symptom of the joint disease, be it acute, recurrent or chronic. Focal infection should, however, not be neglected. His tendency is to accuse constitution, with many others, who see a prevalence of hereditary factors. The diatheses are in their turn made up of climate, environment, occupation, metabolism, age, sex, previous diseases, nutritional habits, *etc.* Pemberton and his co-workers have found that both hypertrophic and atrophic chronic arthritis tend to a slight lowering of metabolism. It is not an inherent defect, but a curtailment of circulation in the tissues, especially of the muscles which are employed in the process of oxidation. With it goes a delay in removal of substances circulating in the blood-stream.—The peripheral blood count of the patients with arthritis shows a diminuation in the number of red blood-cells. The capillary bed seems empty. The amplitude of variation of peripheral temperature is less than in normal persons. This is shown in the rheumatic patient's reaction to cold. Another striking feature found was the elongated colon, widened and tortuous, and inert.—Such findings have pointed to certain therapeutic measures. Metabolism should be increased. The intestinal sluggishness should be overcome, or the bowel emptied, and the diet should supply vitamins. There seems considerable agreement in eliminating more carbohydrates from the diet; high vitamin content is advised with adequate protein, fat to replace the carbohydrates, including cod-liver oil, which has proved beneficial, and the patient should be brought up to an optimum nutrition.—Crowe most emphatically recommends specific vaccine treatment for chronic arthritis and rheumatism, not only as a last resort, but for all cases.—

Kinsella warns that the worst kind of treatment for some of the infectious joints is immobilization. He speaks about the gonococcal form, which he advises, from good experience, to tap and evacuate.

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FLETCHER, A. A.: "The Nutritional Factor in Chronic Arthritis," *J. of Lab. and Clin. Med.*, vol. 15, pp. 1140–1144, 1930.

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LINDSTEDT, FOLKE: "Till kannedomen om de muskelreumatiska (myalgiska) smärtsymtomens natur," *Svensk. Läkares. Handb.*, vol. 54, pp. 145–245, 1928.

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WEIL, MATHIEU-PIERRE: "Quelques cas indiscutables de rhumatismes d'origine dentaire," *La Rev. odontolgique*, vol. 51, pp. 274–287, 1930; "Manifestations articulaires et infectione focale," *Rev. de stomatol.*, vol. 32, pp. 281–291, 1930.

What is done with varicose veins?

Though operations have been quite satisfactory, the fact remains that a surgical intervention is apt to be unpopular. Varicose veins have been injected for the last seventy-five years, and may have been in olden times, if one would make a search for such records. Not all solutions used in the beginning afforded clotting, which was the desired effect, nor were all harmless and painless.—Salt solution, glucose, and salicylate of sodium are contained in the mixture preferred by Bernheim, who injects from five to ten cubic centimeters at a sitting. One starts with one of the veins low down, below the knee, gradually proceeding upward. A tourniquet is not employed, but the patient stands or sits on a table with the legs hanging down. The injected vein bulges and a certain stasis is produced. Sloughs are not as common from glucose and salt, if it should be spilled outside of the blood-vessels, as from other solutions. The needle should be kept very steady, to avoid such deposits, and some blood

sucked up before proceeding with the injection.—Dragos makes a peri-femoral sympathectomy at the Hunterian canal, an incision fifteen centimeters in length, baring the femoral artery for the extent of eight centimeters. He makes a plastic graft after a week and applies compresses of 01.Olivarum 80 and Peru Balsam 20.— Daïnow found that the results of peri-arterial sympathectomy, dilation of the vessels of the extremities, lasted but a few weeks. Scars were fragile. He solves the problem by using acetycholine as a vasodilator. It is a chlorhydrate of acetylcholine stabilized at 5 per cent., using five to ten centigrams per day, or boric acid solutions. Auromatic essences and compresses and ointments are employed locally.

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DRAGOS, AUREL: "Ulcères chroniques de la jambe," *Gaz. des hôp.*, vol. 103, pp. 1104–1108, 1930.

Now what does cause sterility?

Here are two conceptions of the problem. Schorochowa found 2,000 among 10,000 marriages sterile. He believes that examination of the ejaculation slide does not suffice. He made artificial impregnation, morphologic and biologic studies of the semen. The likelihood of fertility was found to be indicated by the proportion of body height and length of testes. All persons with this coefficient below 1/55 were absolutely sterile. The highest coefficient was 1/24, meaning that the length of the testes was contained twenty-four times in the body height. Men with a coefficient of 1/50 to 1/36 were of a dying-out family strain. Some of them had children, but all succumbed young. When they were young these men produced normal sperma, but after a few years azoöspermia was complete. The average coefficient is 1/32; one of 1/29 shows a small number of normal spermatozoa. In those with small coefficient congenital defects were found. In this group the lethal factor was inherited from the parents. These simple measurements, Schorochowa believes, should be used as selective index for progeny. Pathologic spermatogenesis includes oligospermia, oligozoöspermia and mon-

strospermia; furthermore, immobility, or small numbers of motile spermatozoa, *etc.* Though some of the pathologic features of spermatogenesis are found in the ejaculate of normal individuals, they are scarce. This study shows spontaneous abortion, still-births, malformation, and early infant death due to pathologic spermatogenesis. Children of such parents are apt to have testicular hypoplasia, hypospadias, insufficient resistence toward infection, infantilism, *etc.* The very active spermatozoa are more capable of penetrating more rapidly and stay active longer.—Rowe and others attribute sterility to endocrine dysfunction. Among 120 sterile marriages he found more than half with endocrine disturbances. Examination of the genitals, urinary tract and pelvis were made. Furthermore, a careful history was taken, sperma examined, urine, viscosity, metabolism tested. Thus 50 per cent. of the male, and 55 per cent. of the female marriage partners were found to have some endocrine deficiency or disease. Rowe states that this weakness does not, however, constitute the entirety of the problem. There seemed to be a distinct influence of surgical intervention to sterility, though in many instances the pelvic organs were not touched during the operation, as for instance in those who had had operations on tonsils, appendix or adenoids.

ROWE, A. W.: "Endocrine Factors of Human Sterility," *Endokrinologie,* vol. 7, pp. 81–91, 1930.

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The 1930 British Medical Association Meeting at Winnipeg

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The Ninety-eighth Annual Meeting of the British Medical Association was held at Winnipeg, August 26, 27, 28, and 29, 1930. On only two other occasions has the association met outside the British Isles, at Montreal in 1897, when Lister and Osler were present, and at Toronto in 1906.

The main party of British visitors arrived on the *Duchess of Bedford* at Quebec on August 15. On the previous day while passing up the Gulf of St. Lawrence, they sighted the "R-100" on her homeward trip. On August 16 the steamship brought them to Montreal, thence they proceeded to Niagara Falls by train, to Toronto by boat, thence by train to Winnipeg. A second party arrived by the *Duchess of York* at Montreal on August 23 and proceeded to Winnipeg by train. A party of British tuberculosis experts arrived with the main British group, but, on their way West, visited Muskoka and Ninette to investigate sanatoria. The great majority of the visitors to the meeting, including the official delegates from the United States, reached Winnipeg on Monday, August 25.

The United States delegation comprised among others Wm. Gerry Morgan, President of the American Medical Association; E. Starr Judd, President-Elect; Morris Fishbein, Editor, *Journal of the American Medical Association*; Thos. S. Cullen, Baltimore; E. B. Heckel, Pittsburgh; J. H. J. Upham, Baltimore; Rear-Admiral C. E. Riggs, Surgeon-General, United States Navy, Washington, and C. Jeff Miller, President of the American College of Surgeons.

The British Medical Association, with a membership of over 34,000, has branches throughout the British Empire and delegates were present at the meeting from such distant lands as Australia,

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New Zealand, South and East Africa, India, Ceylon, Tasmania, Assam, Mesopotamia and the West Indies.

The headquarters of the meeting were located in the Winnipeg Winter Club. This spacious building housed the Auditorium, seating 2,500, the Pathological Museum, the Commercial Exhibition, the Ladies' Social Club, the Hobbies Exhibit, the Swimming Pool and the Lounges. The scientific sessions, held under fourteen sections, were held in the University of Manitoba, the Legislative Building, the Law Courts and St. Stephens-Broadway Church.

In the words of Sir Chas. Hastings, the founder of the British Medical Association, one of its objects is "Maintenance of the honour and respectability of the profession generally, by promoting friendly intercourse and free communication of its members, and by establishing among them the harmony and good feeling which ought ever to characterize a liberal profession." The annual meetings of the Association, then, are intended to create a spirit of good fellowship among the members and to provide for the free interchange of ideas. Consequently the social side of the meetings ranks in importance with the scientific side and the scientific sessions, which began on the second day of the meeting, lasted only from 10:00 A.M. to 1:00 P.M., the remainder of the day being devoted to clinical addresses or to social events.

The meeting opened with addresses of welcome by the Honorable John Bracken, Premier of Manitoba and Lieut. Col. Ralph H. Webb, Mayor of Winnipeg. Colonel Webb presented a flag of Winnipeg to be hung in the Great Hall of the Association House, Tavistock Square, London. Professor W. Harvey Smith of Winnipeg was inducted as President and invested with the gold chain of office. The Past-President, Mr. Arthur H. Burgess of Manchester, was invested with the Past-President's badge. In the ceremonial meetings of the association there is a flavor of Old World pageantry and color which appeals to the North American eye. The platform was crowded with dignitaries decked in robes in which the scarlet hues of the doctor's degree predominated. The newly appointed Vice-Presidents, Dr. A. D. Blackader of Montreal, the veteran Editor Emeritus of the *Canadian Medical Association Journal*, and Sir Ewen Maclean of Cardiff, a Past-President, were introduced to the President, as were also two Honorary Members, the Archbishop of

Rupert's Land, Primate of All Canada, and Thomas Bassett Mac-Aulay, President of the Sun Life Assurance Company, which has been most generous in the promotion of postgraduate medical education and hospital services in Canada. The President then gave the Presidential Address. After extending a welcome to the visitors and sketching the history of medicine in Canada, he dealt with the economic basis of practice. Many problems were pressing for solution, he said, notably the high cost of medical services, unavailability of medical aid and lack of qualification. Approving reference was made to recent legislation in Alberta providing that no practitioner could hold himself out to the public as a specialist unless he had received from the university of that province a certificate that he had complied with certain specific requirements as to study and experience. High tribute was paid to the work of the Victorian Order of Nurses which operates throughout Canada. The national scope and character of that organization, its uniform policy and methods and its very close association with the medical profession of Canada made it fitting that that body should undertake to solve the problem of nursing cost and service. The problem of placing competent medical skill within reach of all our citizens on a basis that would insure them every care, be just to the members of our profession and satisfy the legitimate demands of the nurse and the hospital could, in his judgment, be solved only by voluntary health insurance, instituted, organized and controlled by the medical profession, and widely applied.

In the afternoon the members donned their academic robes in the Winter Club, proceeded along Broadway to the Cenotaph, where the President deposited a wreath and "Last Post" was sounded, thence to the stately Legislative Building, in front of which an open-air religious service was held. The President read the Lesson and the venerable Primate of All Canada preached on the words, "Luke, the Beloved Physician," declaring that religion and medicine can go hand in hand. Truly, an impressive service.

The President's Reception, held that evening in the Legislative Building, was a blaze of color due to the wearing of academic dress with decorations and medals.

The scientific sessions opened on the second morning. They were grouped in fourteen sections, but in some instances two sec-

tions combined to discuss a subject of importance to both. Thus, on one day, the Section of Surgery met jointly with the Section of Tuberculosis to discuss recent advances in thoracic surgery, and on another day the Section of Diseases of Children met with the Section of Tuberculosis to discuss tuberculosis in children.

The Section of Medicine was presided over by Lord Dawson of Penn, the principal physician of the King in his recent illness, the details of which are given by Dr. J. M. McEachern (Winnipeg) in a special article starting on page 296.

Lord Moynihan of Leeds, President of the Royal College of Surgeons of England, presided over the Section of Surgery. On the opening day, E. W. Archibald (Montreal) discussed "The Scope of Thoracic Surgery," R. A. Young (London) spoke on "Medical Aspects of Thoracic Surgery," A. Tudor Edwards (London) on "Malignant Disease of the Lung," W. L. Mann (Winnipeg) on "Phrenicotomy," J. D. McEachern (Winnipeg) on "Closed Drainage in the Treatment of Empyema," and N. S. Shenstone (Toronto) on "Pulmonary Lobectomy in Bronchiectasis." The second day was devoted to a symposium on the "Uses of Radium in Surgery." The speakers were Sir Charles Gordon-Watson (London), Stanford Cade (London), Douglas Quick (New York), G. E. Birkett (Manchester), Frank Kidd (London) and Hugh Cairns (London). On the third day the discussion was on "Surgery of the Sympathetic Nervous System." W. J. Mayo (Rochester, Minn.) opened the discussion, and was followed by N. D. Royle (Sydney), John Fulton (Oxford), J. R. Learmouth (Rochester), R. B. Wade (Sydney), Wilder G. Penfield (Montreal) and Alfred W. Adson (Rochester). Mr. A. Dickson Wright (London) gave a short paper, "The Treatment of Varicose Ulcer," with cinematographic demonstration.

The Section of Obstetrics and Gynaecology, always well attended, met under the presidency of Mr. Comyns Berkeley of London. As in the preceding section, one morning was devoted to "Radium." The speakers were Sidney Forsdike (London), W. W. Chipman (Montreal) and Malcolm Donaldson (London). Much interest was manifested in the discussion on "The Albuminuria of Pregnancy and Its Late Results," opened by J. Bright Bannister (London), followed by O. Bjornson (Winnipeg), Eric Stacey (Sheffield), Hild-

ing Berglund (Minnesota), Margaret Basden (London) and the President. Professor V. J. Harding (Toronto) described experiments carried on by himself and Dr. H. B. Van Wyck (Toronto) on the effects of hypertonic saline on toxemias of later pregnancy. Salt restriction was a necessary part of prenatal care; protein was harmless. They conceived the toxemias of later pregnancy as due to a fundamental disturbance of water distribution which might be associated with water retention. Dame Louise McIlroy (London) showed two cinematograph films: (1) Classical caesarean section performed at the Royal Free Hospital, London; (2) Method of resuscitation of the newborn in a case of asphyxia after forceps delivery. On the third morning, Professor J. B. Collip (Montreal) spoke on the placental hormone, Emmenine, which he has recently elaborated; Dr. T. G. Stevens (London) gave a demonstration on the operative treatment of prolapse, and Dame Louise McIlroy (London) opened an interesting discussion on the use of sedatives and anesthetics in labor.

The President of the Section of Bacteriology, Pathology, Physiology and Biochemistry was Professor Robert Muir (Glasgow). The discussion on the opening day was on "The Physiology and Pathology of Melanin." Professor James Ewing (New York) opened and was followed by M. J. Stewart (Leeds), Seymour Hadwen (Toronto) and A. T. Cameron (Winnipeg). On the second day, Professor F. T. Cadham (Winnipeg) discussed "Immunological Problems in Septicaemia," and Professors J. B. Collip (Montreal), V. H. K. Moorhouse (Winnipeg), J. C. Meakins (Montreal) and A. T. Cameron (Winnipeg) reviewed the "Physiology of the Parathyroid Glands." The third day's program included papers on "Physiology and Pathology of the Endometrium," by Professor J. H. Teacher (Glasgow), "Intra-epithelial Growth of Carcinoma," by Professor R. Muir (Glasgow), "Coal Miner's Lung," by Professor S. L. Cummins (Cardiff), "The Glioma Group Studied by Ordinary Histological Methods," by Professor Wm. Boyd (Winnipeg), and "The Phosphatase of the Blood Plasma in Bone Dystrophies," by Dr. H. D. Kay (Toronto).

Lack of space forbids extended notice of the remaining sections which also had well-attended meetings with excellent discussions. Among the notable presentations made at these meetings were

"Bacillus Coli Infections," by K. D. Wilkinson (Birmingham) and D. N. Nabarro (London) in the Section of Diseases of Children; "Treatment of Congenital Dislocation of the Hip," by H. P. H. Galloway (Winnipeg) in the Section of Orthopaedics; "The Management and Treatment of Incipient Cataract," by L. V. Cargill (London) in the Section of Ophthalmology; "The Diagnosis of Cancer of the Larynx," by E. D. D. Davis (London) in the Section of Laryngology, and "The Laboratory in a Scheme of Preventive Medicine," by W. G. Willoughby (Eastbourne) in the Section of Public Health. Dr. Willoughby is President-Elect of the association which will meet next year in Eastbourne.

A departure from the usual practice in meetings of the British Medical Association was the insertion on the program of early morning clinics and clinical addresses in the afternoons and evenings. The evening meetings were open to the public and were well attended. On the evening of August 27, Dr. Robert Hutchison (London) spoke on "The Pursuit of Health," and Professor J. E. Gendreau (Montreal) addressed a meeting in St. Boniface in French on "Radium and Cancer." Sir James Purves-Stewart (London) on "Long Life as an Investment." On the following evening Dr. Morris Fishbein (Chicago) gave a racy address on "Foods, Fads and Follies" and Sir James W. Barrett (Melbourne) spoke on the "Bush Nursing System" in Australia. Afternoon addresses were given by Professor W. E. Dixon (Cambridge) on "Drug Addiction," Sir Wm. I. de C. Wheeler (Dublin) on "The Significance of Surgical Recoil in Visceral Decompression," and Dr. Hector Cameron (London) on "Some Functional Nervous Disorders in Childhood." Sir Lenthal Cheatle (London) was prevented by illness from delivering his address, "The Primary Tumour in Carcinoma of the Breast." Morning clinics were given by Dr. John Parkinson (London), "Coronary Thrombosis," Dr. George Riddoch (London), "Organic Nervous Diseases," Dr. Donald Paterson (London), "Coeliac Disease and Pyloric Stenosis," and Mr. Hugh Cairns (London), "Surgical Cases."

It had been wisely determined by the local committee that the entertainment should be distinctive in character. To carry out the idea, seventy-five Indians of the Plain Cree tribe and twenty-five ponies were brought to Winnipeg from Saskatchewan reserves with

the assistance of the Federal Department of the Interior. The Indians pitched their gaily painted tepees at Tuxedo, about three miles from the city, and on the second afternoon of the meeting, before a large gathering, Lord Dawson of Penn was created by the head Cree Chief, Red Dog, a chief of the Cree tribe with the title "Kitche-Okemow-O-Maskikie-Okemow" which signifies "Medicine Man of the Great White Father." The Hon. R. B. Bennett, Prime Minister of Canada, on behalf of the Canadian Medical Association presented to the British Medical Association an enormous buffalo head to be hung in the B. M. A. House, London. The buffalo is the emblem of the province of Manitoba. Afterwards there were a number of Indian pony races. The perfect weather, the gay costumes of the Indians and the famous Mounted Police combined to make a striking picture. Another unique feature was the ice carnival and hockey match on the second evening played on artificial ice at the Amphitheatre rink before 5,000 people. On the final afternoon a garden party was held in Lower Fort Garry, built in 1832, a perfectly preserved stone fort of the Hudson's Bay Company, on the banks of the Red River.

The pathological exhibits, featuring in many instances the results of Canadian research workers such as Banting, Macklin, Archibald, MacKinnon and Nicholson as well as exhibits by British and American scientists, attracted many visitors as did also the Hobbies Exhibit, a collection of paintings, sculpture, wood carving and natural history specimens by medical men. Another exhibit which received many visitors was the Wellcome Historical Museum Exhibit in the Legislative Building.

A special convocation of the University of Manitoba was held on the afternoon of August 28 when the degree of LL.D., *honoris causa*, was conferred upon Lord Dawson, Lord Moynihan, Sir E. Farquhar Buzzard, Sir James W. Barrett, Sir St. Clair Thomson, Mr. A. H. Burgess, Past-President of the Association, Mr. N. Bishop Harman, Treasurer, Professor W. E. Dixon, Dr. W. Harvey Smith, President, Dr. Alfred Cox, Medical Secretary of the Association, and Dr. S. Willis Prowse, Dean of the Faculty of Medicine, University of Manitoba. The venerable Archbishop of Rupert's Land, Chancellor of the University, conferred the degrees.

The annual dinner of the Association was held in the Hudson's

Bay Company building on the evening of August 28.   Over 1,500 guests were present.   After the toast to "The King" had been honored, the following toasts were drunk: "The Empire," proposed by Lord Moynihan of Leeds and responded to by Dr. W. W. White, Mayor of St. John, N. B.; "The British Medical Association," proposed by Dr. W. W. Chipman (Montreal) and responded to by Dr. H. B. Brackenbury, Chairman of Council; "Guests," proposed by Sir St. Clair Thomson and responded to by Wm. Gerry Morgan, M.D., President of the American Medical Association; and "The Ladies," proposed by Professor A. H. Burgess (Manchester) to which Mrs. W. Harvey Smith, the President's Lady, made a witty reply.

Possibly the high-water mark of the meeting was the Listerian oration under the auspices of the Canadian Medical Association delivered by Lord Moynihan on the closing evening before a brilliant audience.   The chairman was Dr. John Stewart of Halifax, N. S., who, like two others present at the meeting, Sir St. Clair Thomson and Mr. L. Vernon Cargill, had been a house surgeon under Lord Lister.   Lord Moynihan is not only an outstanding surgeon but he possesses those qualities of heart, mind, presence and voice which make the true orator.   Arresting phrases sprang from his lips: "Lister, the greatest material benefactor the world has ever known."   "He has saved more lives than all the wars had thrown away."   "Statistics may prove anything, even the truth." "Methods of desperation gave place to measures of deliberation." "Born into the aristocracy of science."   "Ideals are not so much for capture as for pursuit."   "He was both an expert midwife to parturient ideas and their prolific parent."   "Minds subdued by the inertia of old preoccupations."   The oration closed with these words, "What is, nevertheless, so often overlooked is his possession of those qualities; his great heart, his matchless humanity, his unquenchable faith, his flawless intellectual integrity in pursuit of knowledge.   Without his moral sublimity, without the 'soul-making' as Keats called it, Lister could never have changed the face of surgery."

THE SECTION OF MEDICINE OF THE NINETY-EIGHTH ANNUAL MEETING OF THE BRITISH MEDICAL ASSOCIATION

BY JOHN M. McEACHERN, M.D.

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PERHAPS the keynote of the ninety-eighth meeting of the British Medical Association, with its 4,000 physicians of the British Empire and their American guests, is to be found in the sane, careful, somewhat cautious approach to scientific medicine by all the British contributors. Non-essentials were ignored. New fads in treatment or unnecessarily complicated methods were passed by. British medicine appears to be blessed with a directness of view, a forceful clarity of vision, occasionally lacking in other parts of the world.

FILTERABLE VIRUSES

The Section of Medicine had as its president that distinguished physician, Lord Dawson, who introduced the subject of "Filterable Viruses and Practical Medicine."

In an excellent paper, Dr. S. P. Bedson (London), a noted authority on this subject, outlined the nature of filterable viruses. Admitting the living nature of these agents, it was necessary to discover their relation to the bacteria with which we are familiar. The limitations of the microscope add to the difficulty of solving this problem. Certain of the viruses were, however, visible under the ordinary microscope, notably the bodies described by Paschen in vaccina virus and the bodies seen in psittacosis. In his opinion, the available evidence strongly supports the view that filterable viruses are bacterial in nature. It was not entirely true that virus diseases produced a long-standing or life-long immunity. In foot-and-mouth disease and herpes, the immunity was fleeting. Active immunization to virus disease had been practiced for a considerable time in smallpox and rabies. In smallpox a high degree of immunity was obtained by vaccination but the method was not without its dangers. It had been complicated in Europe by an encephalo-

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myelitis of a high degree of mortality. The incidence of this complication was very low, *i.e.*, 1:40,000 vaccinated. It was evident that if the amount of virus introduced was small, this complication could be avoided. Therefore, a small scratch and a very small amount of vaccine virus was recommended.

The use of attenuated virus in the immunization of rabies, originally prepared by drying but now by carbolization, had proved of great value. This principle was now being applied to other virus diseases, namely, foot-and-mouth disease, fowl plague, yellow fever, and distemper. Passive immunity was associated with specific antibodies in the blood—neutralizing antibodies. This principle had been widely used in the prevention of paralysis in poliomyelitis. It was particularly applicable in measles. One to ten centimeters of blood taken early in convalescence and given up to the fifth day of exposure will give complete protection, and the same dose given from the fifth to the eighth day of exposure will modify the attack. In children under two years old, in whom measles is a redoubtable disease, one aims at giving complete protection, but in older children, unless they are delicate, it is better to give partial protection, for the modified measles is a trivial affair and the patient gets the benefit of acquiring a solid immunity to the disease.

IMMUNITY REACTIONS

In virus infections which give rise to specific antibodies, valuable reactions such as the Widal and complement fixation tests are obtained. The flocculation test of Craigie and Tulloch (*Medical Research Council Special Report*, No. 143, 1928) has proved of value in the diagnosis of doubtful cases of smallpox. Doctor Bedson felt that great strides were being made in the fight against virus disease and that there was much hope for the future.

Following this paper, Dr. N. E. McKinnon (Toronto) felt free to mention the work accomplished in Winnipeg during the 1928 epidemic of poliomyelitis which he felt had thoroughly established the value of the intramuscular method of administering convalescent serum. At that time the profession in Canada had had no very adequate knowledge of the pre-paralytic stage of the disease and was only vaguely conscious of the value of convalescent serum. Before the epidemic (475 cases) had well begun, the provincial au-

thorities, University and Medical Societies united to meet the situation. The public and the press were taken into confidence. The people were told the facts and their coöperation was requested, not only in supplying donors but also in calling a physician early in case of sickness. Of fifty-four cases not treated with serum, thirty-four (63 per cent.) showed residual paralysis; six (11 per cent.) died. Of fifty-seven cases treated with serum intramuscularly in the pre-paralytic stage, four (7 per cent.) showed residual paralysis; none died. This is over 90 per cent. complete recovery in the cases treated in the pre-paralytic stage and but 26 per cent. recovery in those not treated. Doctor McKinnon felt that these results were very convincing.

Convalescent serum prophylaxis in measles had not been so extensively used. Measles, in the nine years 1921 to 1929 in Canada, accounted for 5,000 deaths. From the standpoint of mortality, measles was a much more important disease than poliomyelitis. In one infants' home in Toronto previous epidemics of measles had on occasion resulted in a mortality of 24 per cent. Last year sixty-nine children were exposed on three successive nights to a maid suffering from the disease. Blood from convalescents (three to six weeks after recovery) was administered in ten-cubic-centimeter doses five days after exposure. Only five children of the sixty-nine showed very mild abortive symptoms. A maid not given serum developed typical measles fourteen days after exposure.

Doctor McKinnon described the Windsor epidemic of smallpox in 1924. There were sixty-seven cases with thirty-two deaths in one month. Not one of the thirty-two cases that died had ever been vaccinated. The mortality among the unvaccinated was 71 per cent.

The importance of minimum trauma was stressed in vaccination. This means a scratch of one-sixteenth of an inch or less. This is quite sufficient for a good take. Dressings were absolutely contra-indicated. He felt that possibly the minimum trauma method *might* explain the freedom from post-vaccinal encephalomyelitis in the country.

Professor Arthur Ellis (London) felt that the conception of disease must be altered. There was evidence to show that disease occurred in a high percentage of virus carriers, not on account of infection from without, but owing to physical or physiological

changes which took place in the organism, permitting the virus to multiply and overcome the lowered resistance of the individual. He explained post-vaccinal encephalomyelitis on this basis.

Dr. J. C. Meakins (Montreal) described his experience in the treatment of essential hypertension. Following three or four weeks' rest in bed, he had taken blood-pressure readings four times daily and used the average for his results. Ergotamine intramuscularly in 1- to 5-mg. doses had produced a profound but temporary lowering of the blood-pressure and slowing of the pulse (thirty to sixty points for a period of one hour). A more prolonged effect was produced by acetocholine in 0.1- to 0.2-mg. doses in freshly prepared 10 per cent. glucose solution. Seventy-two per cent. of the cases showed a profound drop in blood-pressure. No ill effects had been noted.

FUNCTIONAL DISORDERS OF THE COLON

On the second day Dr. Edmund Spriggs (Ruthin Castle) introduced the subject of "Functional Disorders of the Colon." There had, he said, been no organ about which there had been more difference of opinion in recent times.

Abandoned by Metchnikof as a useless relic, stormed by half a generation of enterprising surgeons who removed large pieces or, when most merciful, stitched it in its presumed place, laved with many waters by physicians and dosed by the public, it had been and was a battlefield with long-drawn-out onslaughts and retreats, the Flanders of medicine. It was indeed fortunate that the large bowel, though easily injured by wrong habits or treatment, had great power of recovery.

In 4,000 cases under Doctor Spriggs' care, a note concerning the colon was made in 2,086. In many the only mention was of delay. In 1,543 some other major or minor abnormality was noted from the symptoms, signs, motions or X-ray examinations. The distribution of the lesions or disorders was as follows: (i) obstruction 19; (ii) parasites 20; (iii) ulcerative colitis and colitis gravis 29; (iv) dysenteries 29; (v) growths 32; (vi) loops and redundancies 45; (vii) colectomy, colostomy and colopexies 51; (viii) adhesions, largely post-operative, 85; (ix) mucous and mucomembranous colitis 164; (x) coloptosis 202; (xi) diverticulosis and

diverticulitis 297; (xii) disorders of tone and segmentation 570 (including 198 with excessive tone and spasm). This group includes also eighty-four cases of irritable colon with prominent clinical symptoms but little or no mucus.

For the purpose of this discussion, organic lesions including ulcerative colitis and colitis gravis, that is, with inflammation of the lining, seen with the sigmoidoscope, were excluded. The cases of mucous and membranous colitis in which no pus, or pus mixed with blood was passed, are included; .also cases of irritable colon, coming under the heading of disorders of tone, in which the symptoms from the colon were most prominent and gave X-ray evidence clear, among them cases of nervous diarrhea.

The main groups of conditions classed as functional are therefore *colonic delay* or constipation, *irritable colon*, including *nervous diarrhea, spastic colon*, mucous colitis or catarrh of the colon and *mucomembranous colitis*. The word colitis is not correct but is used.

Coloptosis was discussed and the opinion expressed that as a rule it does not matter where the colon lies so long as it passes on its contents normally. Of 141 consecutive cases of coloptosis, in fifty-five the rate of passage of the barium meal was normal, and in thirty-five others the delay was moderate only. Hence, in more than half retardation was inconsiderable. In 27 per cent. there was great delay. Symptoms arose from dropping *per se* in severe cases only.

Under the heading of coloptosis were sixty-six other cases with colitis, diverticulitis or other disease of the colon. These were not added in as they would have been counted twice.

Next came an outline of the functions of the normal colon, including its radiology (O. A. Marxer), with illustrations and average measurements of rate of passage, length and capacity.

Etiology.—Infections, parasites, exposure and other injuries were mentioned and the two main causes, neurosis and constipation, discussed. It was suggested that the usual treatment for constipation, namely, irritating aperients, taken over long years, is as potent and frequent a cause of colitic disorder as constipation itself; and this is confirmed by the good result of withdrawal. An analysis of 1,000 cases of radiological delay under the speaker's care was quoted and supported the views expressed. Of these, 236 were unaware

of constipation and 764 complained of it. Of the latter, 670 were taking aperients, 436 every day.

The association of other alimentary disorders with functional disease of the colon was laid stress on. In 242 cases of mucous colitis and irritable colon, in roughly half there was or had been some other lesion or suspected lesion of the alimentary tract. These lesions were analyzed, the most prominent being appendicitis, disease of the gall-bladder and ulcers of stomach or duodenum. Hence all these cases should be observed carefully, and the practice of operating first and investigating afterward avoided.

Under the heading of *pathology*, the powers of resistance of the mucous membrane to harmful agencies and its vulnerability were discussed. The view was put forward that sluggishness of the bowel leads to venous stasis, with diminished absorption of gas, and that interference with motility may be a cause of flatulence more than the usually alleged fermentation.

Under *morbid anatomy* redundant loops were discussed and their bacteriology reviewed, stress being laid on the lack of experimental grounds for indiscriminate vaccines. The estimate of what value they may have rests on a clinical and not on a scientific basis. Statistics of cultures were quoted, showing that streptococci were less common in constipated motions and more so in loose ones. From the results of 2,000 cultures it appeared that in the present state of our knowledge, repeated culture of the motions in these disorders, after the preliminary diagnostic examination for organisms known to be pathogenic, was not worth the labor and cost involved in performing them.

Then followed an analysis of the *symptoms, signs, faeces, radiologic* and *sigmoidoscopic* appearances in the 242 cases. The chief symptoms were: abdominal pain or discomfort; poor appetite; nausea; and vomiting. Constipation is usual and many complaining of diarrhea show with X-rays delay in the bowel. The incidence was also given of weariness, depression, headache, malaise, palpitation, heart pains, shivering and cold hands and feet.

Among signs it was mentioned that in 111 cases the gastric juice was superacid in 41 per cent., subacid in 23 per cent., achlorhydric in 2 per cent.

As regards colonic delay, proved radiologically, in the 1,000 cases quoted (analyzed by R. Picton-Davies) the delay was in the whole colon in half the cases, and in the sigmoid or rectum, or both, in one-third. Cecal delay alone was rare (1 per cent.) and often means local inflammation. Two hundred and eighty-nine complained of headache and 181 were depressed or neurasthenic.

Diagnosis.—The diseases most likely to be confused are (1) those causing dyspepsia, such as gastritis, gastric and duodenal ulcer, gall-stones and appendicitis; (2) the dysenteries, colitis from parasites, diverticulosis and diverticulitis, and chronic obstruction from organic causes, especially cancer; (3) diseases arising from without the colon, achylic and pancreatic diarrhea, Graves' disease, diseases of the ovaries, tubes or womb, nor forgetting prolapse, and sometimes renal colic.

The usual examinations for other conditions should always be made. Stress was laid upon inspection of the motions.

Under the heading *prophylaxis* comes the hygiene of the normal colon. The main rules of *treatment* are: to allay anxiety, to abolish laxatives and purges, to give a suitable diet and to regulate rest and exercise. In severe cases it may be necessary to remove the patient for a long period from surroundings in which the derangement arose. The patient often is convinced that it is harmful for material to lie in the colon for more than forty-eight hours; that if an action does not take place in the morning an aperient should be taken that evening, that the large semi-fluid motions produced by aperients, to yield which a great part of the colon is emptied, are beneficial; that an ordinary formed motion due to the emptying of the lower sigmoid is not enough; that abdominal disorder and loss of vitality are lessened by the use of aperients. It was suggested that these opinions are in the main wrong, and reasons given.

Diet suitable for different cases varies from a bland one in severe cases (used in 42 per cent. of this series) to a rougher diet in milder ones. The use of paraffin, massage, baths, intestinal douches, exercise, electrical treatments, rest (including mental rest) and other measures were discussed.

Of *drugs*, belladonna, hyoscyamus, arsenic, intestinal antiseptics, castor oil and salines were discussed, also special measures for severe mucous colitis, spastic cases and nervous diarrhea.

Surgery.—Experience of surgical operations for functional disorders of the colon is unconvincing. The results of colectomy, short-circuiting operations and colopexy were discussed. No operation has been devised, or will be, which will make a man out of training fit to run a race. In these patients the bowel is out of training and surgery as a means of restoring its powers is usually futile.

The *results* of the treatment of 208 cases are quoted: 34 per cent. were treated in bed at first, 64 per cent. with douches, 11 per cent. with castor oil. In 90 per cent. much benefit was obtained from a course averaging 6.7 weeks in length. Each patient should receive and follow detailed instructions on returning home.

The paper was illustrated by lantern slides and recital of cases. The speaker concluded, "These diseases do not kill; but they cause weakness and misery. If we can educate ourselves and the public in regard to the hygiene of the colon, a great addition will have been made to human health and happiness."

In the discussion which followed Doctor Spriggs' paper, Dr. Thos. McRae (Philadelphia) emphasized the abuse of laxatives and the neurotic element in these cases. Many fads in treatment had risen, especially in the United States. Reflex causes of spasm of the colon should not be lost sight of, such as prostatitis.

Lord Dawson felt that colitis was a colonic expression of deranged function elsewhere. The spare, highly strung individuals with flat abdomens were most often the victims of this complaint. They became "abdominal conscious." The strain of modern life became concentrated in their abdomens. The chief thing was to bring the abdomen out of their realm of consciousness. To do this they must first of all avoid anxiety, cold, fatigue, and hunger. Detailed diets and strict régimes made them worse by centering attention upon the abdomen.

ACUTE POLIOMYELITIS

On the third day Sir Farquhar Buzzard, the successor of Osler in the Regius Chair of Medicine at Oxford, opened the discussion on acute poliomyelitis. One of the great problems for solution was to determine the method of spread in the community. Direct contact was accepted as a possibility, but that carriers were responsible for epidemics was more likely. Until we had practical methods for

As regards colonic delay, proved radiologically, in the 1,000 cases quoted (analyzed by R. Picton-Davies) the delay was in the whole colon in half the cases, and in the sigmoid or rectum, or both, in one-third. Cecal delay alone was rare (1 per cent.) and often means local inflammation. Two hundred and eighty-nine complained of headache and 181 were depressed or neurasthenic.

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distinguishing between natural and acquired immunity, the problem was not likely to be solved.

Many carriers were immune to the disease. If a test for the virus for all cases of pyrexia of unknown origin could be found, the solution would be simple. Not much advance could be made until a biological test for early diagnosis had been discovered.

Dr. H. B. Cushing spoke of the encouraging results of convalescent serum therapy in Canada.

The writer of this article gave the results of the Medical Research Committee in the Manitoba epidemic of 1928 as shown in the following table:

Group	Number of cases	Number completely recovered	Per cent. completely recovered	Number showing residual paralysis	Per cent. residual paralysis	Deaths No.	Deaths Per cent.
I......	57	53	93	4	7	0	0
II......	17	16	94	1	6	0	0
III......	33	7	22	15	45	11	33
IV......	54	14	26	34	63	6	11

Group I—One dose intramuscular serum in pre-paralytic stage.
Group II—Two or more doses of serum by various routes (pre-paralytic stage).
Group III—Serum given after onset of paralysis.
Group IV—No serum given.

The necessity of early diagnosis of the disease was emphasized. The following modification of a description of the pre-paralytic stage by Aycock and Luther was used extensively during the epidemic.

The onset is sudden and abrupt with a rapid rise in temperature which is usually under 102° F. The degree of prostration is greater than would seem justified by the temperature. Vomiting may occur, usually only once, and that shortly after the onset. The child may complain of frontal headache, sore neck or lumbar pain. Pain in the limbs is common. The child is irritable and restless—or may be drowsy. A fine tremor of the hands or a muscular twitching has been noted. The face is flushed, the expression anxious and there is often a peculiar, dazed expression somewhat similar to that observed in a slight cerebral concussion. The pulse is usually

rapid, out of proportion to the temperature. The respirations are at times increased in rate. There is frequently rather a coarse intention tremor. There is a distinct rigidity of the neck. The head can be brought about halfway forward when resistance is encountered and the child complains of pain. The spine sign is usually positive. This sign may be demonstrated in two ways. In small children the hands are placed under the shoulders and buttocks and the child lifted horizontally from the bed. In positive cases the spine is held rigid, sometimes defensively arched. Any attempt to bend the spine causes pain. Older children raise themselves to a sitting posture with difficulty and are unable to bend forward except from the hips, when asked to touch their toes. A cerebrate tache is frequently present but it is also frequently present in other febrile diseases. The reflexes are disturbed in some way in nearly every positive case. In 34 per cent. of our cases there was absence of the abdominal reflexes. One or both ankle-jerks may be absent. Kernig's sign is frequently positive and the manipulation may cause pain along the spine. The knee-jerks are absent (35 per cent.) or exaggerated (18 per cent.) in some cases. We feel that any variation or slight abnormality of the reflexes during the early stage of an acute febrile illness, combined with a stiff neck or spine, justifies a diagnosis of poliomyelitis. A spinal fluid cell count is essential at this stage.

It is felt that this procedure is as important and as necessary in the diagnosis of poliomyelitis as the leukocyte count is in a patient with suspected inflammation of the appendix.

Dr. R. G. Armour was impressed by the frequency of gastro-intestinal symptoms in the pre-paralytic stage. He felt that in many cases in which a large dose of castor oil was administered in the pre-paralytic stage, the acute phase was never so severe or the sequelae so serious. Rest during the acute stage was essential in his opinion.

Dr. A. Gibson (Winnipeg), speaking on the orthopaedic aspects of the subject, sounded a note of warning against the use of vigorous massage and electrotherapy in these paralyzed children. He advocated rest, the prevention of deformity and gentle stimulation by skin stroking.

CUMULATIVE INDEX

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(The Roman figures, i, refer to Volume I [March]; ii, to Volume II [June]; iii, to Volume III [September]; and iv to Volume IV [December]; and the Arabic figures, to the page in which the reference will be found.)